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CORRESPONDENCE

Alopecia areata following pembrolizumab: A case report and literature review

To the Editor,

The skin immune reaction is essential to eradicate malignancies derived from the host human body.[1] Since malignancies develop their escape strategy from anti-tumor immunity mediated by programmed cell death 1 (PD-1)/programmed cell death ligand 1 (PD-L1) or CTLA-4, the recent advancement of immune checkpoint inhibitor treatment proves the importance of immune reaction against malignancies.[2] On the other hand, healthy human tissue or organs also need to tolerance mechanism escaping from immune reactions not to cause excessive inflammatory reactions.[3] Therefore, these immune escape molecules are also required for healthy subjects. Herein, we report a case of alopecia areata following pembrolizumab administration and also review the previously published cases of alopecia areata following PD-1/PD-L1-targeted therapy further.

A 73-year-old male continued to receive pembrolizumab for his advanced bladder carcinoma and recognized hair loss lesions on his scalp which were gradually developed 6 months after the pembrolizumab treatment. On physical examination, round shape hair loss lesions were observed on his scalp (Figure 1A). A skin biopsy taken from his hair loss lesion revealed inflammatory cell infiltration around the bulge of hair follicles (Figure 1B). The infiltrating inflammatory cells are a mixture of CD4+ or CD8+ cells (Figure 1C, D).

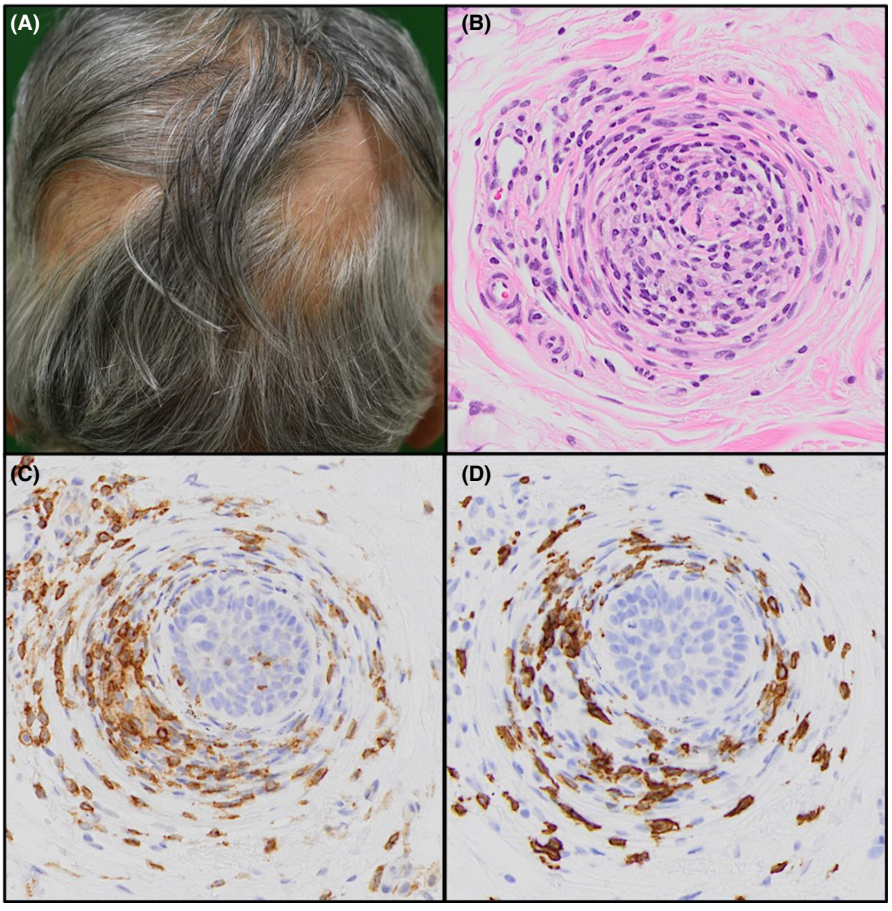

FIGURE 1 Clinical manifestation and histological analysis (A) a clinical manifestation of this patient. (B) Hematoxylin and eosin staining. (C) Immunostaining for CD4. (D) Immunostaining for CD8

Because pembrolizumab treatment was essential for his advanced bladder cancer, the treatment was continued. In addition, topical application of steroid and phototherapy were administrated for 2 months showing a partial response of hair growth.

A hair follicle exhibits immunity privilege construction.[4] MHC class I and CD200 are representative immune regulatory factors.[5,6,7] The break of these molecules is observed in patients with alopecia areata. PD-L1 also plays a role in the immune privilege function in hair follicles. As the reason why PD-1-targeted therapy is involved in the development of alopecia areata, it seems to be depending on the PD-1 expression in the bulge of hair follicle for the immunological escape phenomenon of hair follicle. PD-L1 is upregulated in dermal sheath cup cells.[8] PD-L1 is essential for immune escape phenomenon and consistently anti-PD-L1 antibody treatment becomes a trigger to cause alopecia areata.

To evaluate the characteristics of alopecia areata following immune checkpoint inhibitors, 23 cases of alopecia areata following immune checkpoint inhibitor treatment were reported (Table S1). Although the severity of alopecia according to CTCAG 5.0 classification does not seem to be more severe in the combination immunotherapy, careful observation is required during the treatment. More than half of patients showed an improved response, suggesting that it might be better to continue immune checkpoint inhibitor even though encountering the development of alopecia. Although no significant differences were observed, the duration of alopecia areata onset and the duration until improvement seemed to be shorter in patients with ICI combination therapy. To conclude the accurate outcomes, it is necessary to clarify the detailed characteristics of alopecia areata following ICI by the accumulation of case series studies, and these patient's characteristics will become helpful information for clinicians.

DECLARATION SECTION

Approval of the research protocol: No.
Informed Consent: N/A.
Registry and the Registration: N/A.
Animal Studies: N/A.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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