Received: 13 January 2022 | Revised: 24 February 2022 | Accepted: 31 March 2022

DOI: 10.1002/cia2.12244

Journal of Cutaneous Immunology and Allergy

WILEY

CORRESPONDENCE

Exacerbation of pre-existence psoriasis following immune checkpoint inhibitor treatment

Immune checkpoint inhibitors (ICI) are currently developed for the treatment of cancers showing high efficacy even in the cases of advanced and persistent malignancies.[1] On the contrary, autoimmune adverse reactions are recognized during ICI treatment.[2] The brake of skin tolerance exacerbates excessive inflammatory reactions,[3] and ICI treatment impairs skin tolerance mechanisms.[4,5] Indeed, skin toxicities are one of the most common immune checkpoint inhibitor-related adverse events (irAE), such as maculopapular rashes, lichenoid dermatitis, bullous pemphigus, and vitiligo.[6] Psoriasis has also been reported as a rare irAE in both the exacerbation of pre-existing psoriasis and the novel onset psoriasis during immunotherapy. However, the detailed characteristics of these differences remain unclear. Herein, we report a case of pre-existence psoriasis, which was exacerbated following the administration of ICI. We also summarize case reports and conducted a review of the literature.

A 63-year-old man was suffered from advanced renal clear cell carcinoma and was treated with nivolumab 240 mg every 2 weeks following 4 cycles of immunotherapy with ipilimumab 80 mg plus nivolumab 240 mg. At the time of presentation, the treatment had been administered for 5 times. Although he had chronic plaque psoriasis 5 years prior to the administration of ICI, his psoriasis was under control without any treatment. The physical examination revealed a generalized distribution of scaly erythematous papules and plaques on his trunk and extremities. A skin biopsy showed parakeratosis with acanthosis and a hypogranular layer in the epidermis. Lymphocyte cell infiltration was also observed in the papillary dermis. Based on the clinical manifestation and histological examination, we diagnosed his skin eruption as psoriasis vulgaris. His skin eruption was well responded to topical corticosteroids and vitamin D analogs under nivolumab treatment. The tumor size was reduced after 4 cycles of immunotherapy with ipilimumab plus nivolumab. However, the tumor progression was observed 8 months after the administration of ICI.

IL-17-producing helper T cells (Th17) are recognized as a central player in the pathogenesis of psoriasis.[7] PD-1 suppression enhances Th17 activation and secondary overproduction of IL-17.[8,9] Therefore, it is reasonable to cause both the novel onset of psoriasis and the exacerbation of pre-existence psoriasis during anti-PD-1/PD-L1 antibody treatment. However, it is assumed that pre-existence psoriasis has already established a more mature form of pathogenesis, possibly leading to the risk of discontinuation of ICI treatment due to persistent psoriasis skin inflammation. To clarify this hypothesis, we summarized a case of psoriasis associated with ICI treatment, especially anti-PD-1/PD-L1 antibody treatment (Table 1). We noticed a higher frequency of discontinuation or interruption of an immune

TABLE 1 Immune checkpoint inhibitor-related psoriasis[9-30]

	Psoriasis	
	Pre-existence	**Novel**
Number	27	22
Mean age	64.2	68.1
ICI treatment	Nivolumab: 19 Pembrolizumab: 5 Duralumab: 2 Atezolizumab: 1	Nivolumab: 17 Pembrolizumab: 5
Discontinuation or interruption of ICI	Total 11 cases (40.7%) Psoriasis 7 cases (25.9%) Tumor progression 1 case (3.7%) Pneumonia 1 case (3.7%) Unknown 2 cases (7.4%)	Total 6 cases (27.2%) Psoriasis 5 cases (22.7%) Unknown 1 case (4.5%)

checkpoint inhibitor in patients with pre-existence psoriasis; however, there was no big difference in discontinuation or interruption of ICI between the patients with pre-existence psoriasis and those without psoriasis. Therefore, we could not conclude whether the pre-existence of psoriasis needs to be more carefully observed in our literature review analysis. It is necessary to conduct strength topical or systemic therapy against psoriasis such as apremilast[10] to avoid discontinuation or interruption of immune checkpoint inhibitor treatment.

DECLARATION SECTION

Approval of the research protocol: N/A.
Informed Consent: N/A.
Registry and the Registration: N/A.
Animal Studies: N/A.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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