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CORRESPONDENCE

A case of readministration of nivolumab by treating with apremilast for psoriasiform eruption as irAE

Dear Editor,

The wide use of nivolumab in various cancer cases has led to several reports of nivolumab-induced psoriasiform eruption. We report a case in which nivolumab was readministered with apremilast to overcome psoriasiform eruption caused by nivolumab.

An 81-year-old Japanese man with renal cell cancer (cT3N0M1) was referred to our hospital for scaly erythema on the extremities. He had been diagnosed with right renal cell cancer 12 years previously and had undergone a right nephrectomy. Lung metastases were also resected the same year, but multiple lung metastases reappeared 4 years later. He had progressive disease, despite undergoing chemoradiotherapy. Therefore, he was treated with nivolumab.

Six months after nivolumab administration, scaly erythema appeared on his head, back, and extremities (Figure 1A-C), and the biopsy from erythema on his leg showed parakeratosis, epidermal hyperplasia with elongated rete ridges and dilated blood vessels at the tip of the dermal papillae. We diagnosed him with psoriasis based on these findings. The erythema was not improved by treatment with topical steroids. His Psoriasis Area and Severity Index (PASI) score was 7.8 and his Dermatology Life Quality Index (DLQI) score was 4 points.

Five months after his first visit, nivolumab was discontinued due to exacerbation of dactylitis. His PASI score decreased by 3-5 points after discontinuation, but the dactylitis and nail lesions remained (Figure 1D).

He also had severe renal dysfunction, and apremilast was started after initiation of dialysis. His PASI score changed to almost clear and his nail lesions and dactylitis improved (Figure 1E).

Nivolumab was resumed eight months after withdrawal due to enlargement of the lung metastases. However, his PASI and Nail

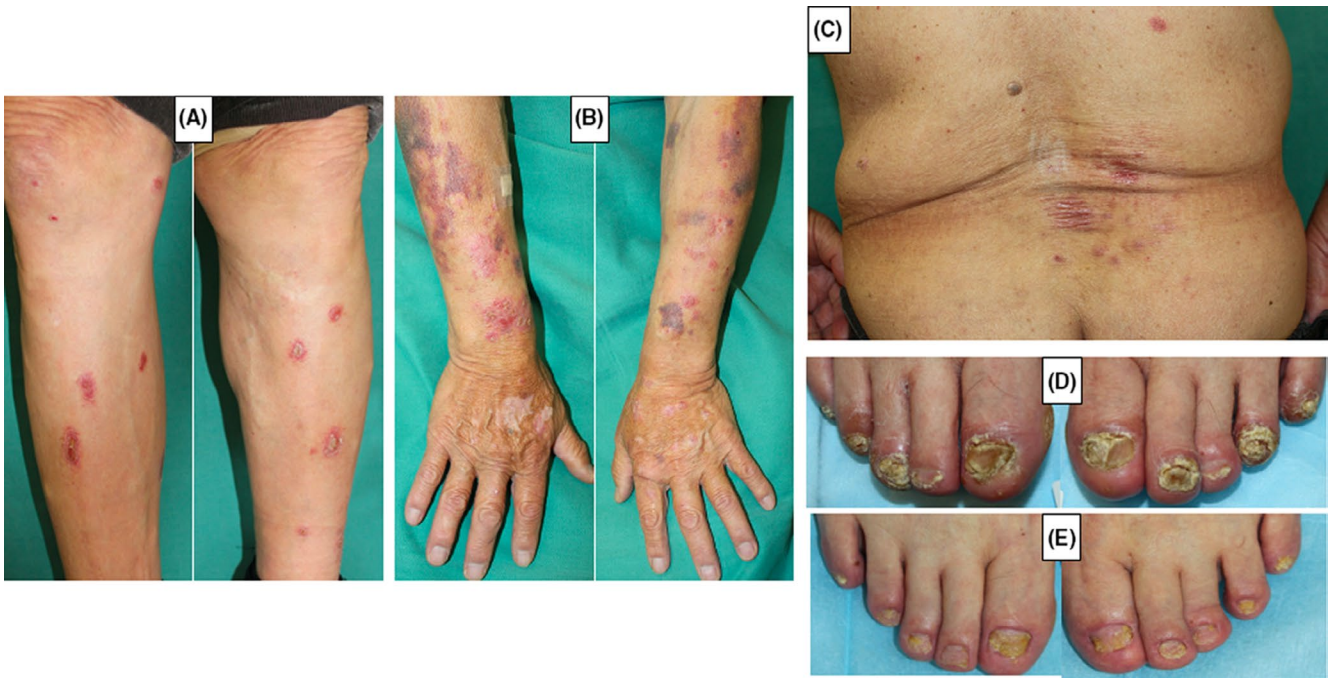

FIGURE 1 (A-C) scaly erythema on the back and extremities. (D) Dactylitis and nail lesions before initiation of apremilast (NAPSI score 4.8 points). (E) Dactylitis and nail lesions improved 1.5 years after apremilast administration; (NAPSI score 1.5 points)

Psoriasis Severity Index (NAPSI) scores did not worsen, and the metastasis became stable disease.

As of November 30, 2020, 2337 cases of nivolumab-related skin damage were reported, including 108 psoriasiform eruption cases.[1] Many clinical forms were plaque and drop-shaped types.[2] Psoriasiform eruption treatments included topical medications, phototherapy, etretinate, cyclosporine, oral prednisolone, antihistamines, and apremilast.[3]

PD-1 inhibitors enhance Th1/17-type responses,[4] and serum IL-6 levels can be elevated by immune-related adverse events (irAEs) with nivolumab. IL-6 is implicated in this pathology through induction of Th-17 and promotion of inflammation and thickening of the skin, but the detailed mechanism is unknown.

In clinical trials in Japan and overseas, the relationship between apremilast administration and the development of malignant tumors cannot be denied.[5,6] Thus, apremilast may be involved in tumor immunity. Conversely, Kahn et al.[7] reported no tumor recurrences in 16 patients with malignant tumors who underwent psoriasis treatment with apremilast, biologics, or both. Other clinical trials[8] have also shown similar incidences of malignant tumors in placebo and apremilast groups. As in the present case, when psoriasiform eruptions appeared following nivolumab treatment, nivolumab could be resumed after apremilast treatment. Therefore, in cases of moderate or more psoriasiform eruptions caused by nivolumab, apremilast may be a treatment option, although more cases need to be accumulated.

CONFLICT OF INTEREST

The authors declares no conflict of interest.

DECLARATION SECTION

Approval of the research protocol: N/A.

Informed Consent: Written informed consent was obtained from the patients.

Registry and the Registration No. of the study/trial: N/A.

Animal Studies: N/A.

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REFERENCES

1. Opdivo.jp [internet]. Ono Pharmaceutical Co.; [updated Nov 2020]. https://www.opdivo.jp/system/files/2020-12/side_effect_2.pdf. Accessed 4 Jul 2014
2. Bonigen J, Raynaud-Donzel C, Hureaux J, Kramkimel N, Blom A, Jeudy G, et al. Anti-PD1-induced psoriasis: a study of 21 patients. J Eur Acad Dermatol Venereol. 2017;31:e254–7.
3. De Bock M, Hulstaert E, Kruse V, Brochez L. Psoriasis vulgaris exacerbation during treatment with a PD-1 checkpoint inhibitor: case report and literature review. Case Rep Dermatol. 2018;10:190–7.
4. Imai Y, Ayithan N, Wu X, Yuan Y, Wang L, Hwang ST. Cutting edge: PD-1 regulates imiquimod-induced psoriasiform dermatitis through inhibition of IL-17A expression by innate γδ-Low T cells. J Immunol. 2015;195:421–5.
5. Paul C, Cather J, Gooderham M, Poulin Y, Mrowietz U, Ferrandiz C, et al. Efficacy and safety of apremilast, an oral phosphodiesterase 4 inhibitor, in patients with moderate-to-severe plaque psoriasis over 52 weeks: a phase III, randomized controlled trial (ESTEEM 2). Br J Dermatol. 2015;173:1387–99.
6. Ohtsuki M, Okubo Y, Komine M, Imafuku S, Day RM, Chen P, et al. Apremilast, an oral phosphodiesterase 4 inhibitor, in the treatment of Japanese patients with moderate to severe plaque psoriasis: efficacy, safety and tolerability results from a phase 2b randomized controlled trial. J Dermatol. 2017;44:873–84.
7. Kahn JS, Casseres RG, Her MJ, Dumont N, Gottlieb AB, Rosmarin D. Treatment of psoriasis with biologics and apremilast in patients with a history of malignancy: a retrospective chart review. J Drugs Dermatol. 2019;18:387–90.
8. Boffetta P, Gridley G, Lindelöf B. Cancer risk in a population-based cohort of patients hospitalized for psoriasis in Sweden. J Invest Dermatol. 2001;117:1531–7.

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