CORRESPONDENCE



Case of durvalumab-induced annular psoriasiform dermatitis in lung cancer

A 69-year-old Japanese man was diagnosed with liver metastases (Stage III) from non-small-cell lung cancer, and durvalumab administration was started. The patient had no history of medication that could have induced psoriasis. After two cycles of durvalumab, scaly erythema appeared on the palms. After 4 cycles of durvalumab, interstitial pneumonitis developed, so durvalumab administration was discontinued, and oral prednisolone was started, and the erythema became pigmented. After the resumption of durvalumab administration, scaly annular erythema appeared on the head and face. After 14 cycles of durvalumab, Trousseau syndrome developed, and durvalumab administration was discontinued, but the erythema expanded.

The clinical findings at the first visit were scaly annular erythema (Figure 1A,B) on the head and face, scaly erythema on the abdomen (Figure 1C), and diffuse erythematous plaques (Figure 1D,E) on the fingers and soles of the feet. There were no nail or joint lesions, and no fungi were detected on the erythematous plaques. A skin biopsy of the scaly annular erythema on the head showed hyperkeratosis with parakeratosis and thickening of the epidermis, loss of the granular layer, and perivascular infiltration of lymphocytes on the upper dermis (Figure 1F). Lymphocytes had infiltrated the epidermis, keratinocyte apoptosis was observed, and there were psoriasis-like epidermal changes. A skin biopsy of the abdominal erythema showed similar results.

Immunohistochemically, CD4-positive T cells had mainly infiltrated the region around the dermal blood vessels, and there was little infiltration into the epidermis (Figure 1G). In addition, many TIA-positive cells and CD8-positive T cells had infiltrated sites where necrosis of keratinized cells was observed in the epidermis (Figure 1H,I). Local calcipotriol hydrate betamethasone dipropionate and narrowband ultraviolet B phototherapy caused pigmentation of the annular erythema on the head after approximately one month. However, he died due to respiratory failure 15 months after the start of durvalumab administration.

Immune checkpoint inhibitors (ICIs) have been shown to be effective in a variety of cancers. Durvalumab is an anti-PD-L1 monoclonal antibody that is indicated for the treatment of unresectable stage III non-small-cell lung cancer. There have been many reports of psoriasiform dermatitis with anti-PD-1 antibodies, but none of these cases developed annular erythema. There have been four cases of psoriasiform dermatitis due to anti-PD-L1 antibodies, only one of which was scaly annular erythema. There was no history of psoriasis, and topical steroid and narrowband ultraviolet B phototherapy were used in the previous report.

In this case, scaly annular erythema on the head showed histopathological psoriasis-like epidermal thickening and sites where necrosis of epidermal keratinized cells was observed as the infiltration of many CD8-positive T cells and TIA-positive cells was seen. It was

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FIGURE 1 Clinical appearance and histological findings of the patient. (A, B) The patient presented with scaly annular erythema on the head and face. (C-E) Scaly small erythema on the abdomen and diffuse scaly erythematous plaques on the fingers and soles were distributed. (F) A skin biopsy of the annular lesion on the head revealed hyperkeratosis with parakeratosis and thickening of the epidermis, loss of the granular layer, and perivascular infiltration of lymphocytes on the upper dermis. Lymphocytes had infiltrated the epidermis, and keratinocyte apoptosis was sporadically observed. The bar indicates $100\,\mu\text{m}$. (G-I) An immunohistochemical analysis for anti-CD4 (G), anti-CD8 (H), and anti-TIA (I) revealed that lymphocytes had infiltrated around the small vessels of the upper dermis. The bar indicates $100\,\mu\text{m}$

reported that anti-PD-1 antibodies induced the activation of T cells including Th1 and Th17 cells triggering epidermal thickening and Th9 cells triggering cytotoxic effect.^{4,5} Therefore, it was suggested that durvalumab also has induced psoriasiform dermatitis that was also associated with histopathological keratinocyte apoptosis by the activation of these T cells.

DECLARATION SECTION

Approval of the research protocol: No human participant was involved in this study.

Informed Consent: N/A.

Registry and the Registration No: N/A.

Animal Studies: N/A.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

Asako Ota MD¹
Saori Itoi-Ochi MD, PhD¹

Mami Hayashi MD¹

Akiko Miyazaki MD¹

Masaki Miyazaki MD, PhD²

¹Department of Dermatology, Suita Municipal Hospital, Suita, Japan

²Department of Respiratory Medicine and Clinical Immunology, Suita Municipal Hospital, Suita, Japan

Correspondence

Saori Itoi-Ochi, Department of Dermatology, Suita Municipal Hospital, 5-7 Kishibeshinmachi, Suita, Osaka 564-8567,

Japan.

Email: ochi0666@mhp.suita.osaka.jp

ORCID

Saori Itoi-Ochi https://orcid.org/0000-0002-8646-2059

REFERENCES

- Tattersall IW, Leventhal JS. Cutaneous toxicities of immune checkpoint inhibitors: the role of the dermatologist. Yale J Biol Med. 2020;93(1):123-32.
- Geisler AN, Phillips GS, Barrios DM, Wu J, Leung DYM, Moy AP, et al. Immune checkpoint inhibitor-related dermatologic adverse events. J Am Acad Dermatol. 2020;83(5):1255-68.
- Lin WH, Lee KY, Lee WR, Shin YH. Durvalumab-induced de novo annular psoriasiform drug eruption successfully treated with a combination of narrowband ultraviolet B phototherapy and topical treatment. J Dermatol. 2020;47(9):1041–5.
- Dulos J, Carven GJ, Boxtel SJ, Evers S, Driessen-Engels LJA, Hobo W, et al. PD-1 blockade augmentsTh1 and Th17 and suppresses Th2 responses in peripheral blood from patients with prostate and advanced melanoma cancer. J Immunother. 2012;35(2):169-78.
- Nonomura Y, Otsuka A, Nakashima C, Seidel JA, Kitoh A, Dainichi T, et al. Peripheral blood Th9 cells are a possible pharmacodynamic biomarker of nivolumab treatment efficacy in metastatic melanoma patients. Oncoimmunology. 2016;5(12):e1248327.