Sarilumab-induced cutaneous adverse event

Dear Editor,

IL-6 is a representative inflammatory cytokine leading to inflammation, cell differentiation, and proliferation. Therefore, the blockade of this cytokine signaling is expected to show beneficial potent in various inflammatory diseases, such as rheumatoid arthritis. Although tocilizumab is a firstly available humanized monoclonal antibody against IL-6R subunit IL-6Rα, sarilumab is a fully human monoclonal antibody against IL-6Rα antagonist and blocks IL-6 signaling in various inflammatory diseases, especially used for the treatment of rheumatoid arthritis. There, several adverse reactions have been reported during IL-6R-target treatment, such as infection and cutaneous adverse reactions. Herein, we report the first case of cutaneous adverse events due to sarilumab in a patient with rheumatoid arthritis.

An 80-year-old man suffered from rheumatoid arthritis and sarilumab was administrated for his refractory rheumatoid arthritis. He first recognized erythema on the bilateral soles, which were improved several days after the 5th administration of sarilumab. He again experienced this recurrent skin eruption after the 6th sarilumab administration and gradually developed. Physical examination showed scaly erythematous plaques on his hand, foot, and lower extremities (Figure 1A, B). He also received sulfamethoxazole for the prevention against pneumocystis carinii pneumonia during sarilumab treatment. There was no history of psoriasis and palmoplantar pustulosis. A skin biopsy taken from his foot eruption showed parakeratosis and acanthosis with hypogranular layer and lymphocyte infiltration in the dermis. A pustule formation was also observed in the epidermis (Figure 1C). KOH test was a negative result. Although he was received sarilumab in addition to sulfamethoxazole during the appearance of a cutaneous adverse event, his skin eruption was dramatically improved after the topical application of calcipotriol hydrate and betamethasone dipropionate and the discontinuation of sarilumab even though the continuation of sulfamethoxazole. Therefore, we diagnosed his skin eruption as a sarilumab-induced cutaneous adverse event. His treatment for rheumatoid arthritis was switched to golimumab without the recurrence of skin eruption.

Although this is the first case report showing a cutaneous adverse event due to IL-6Rα inhibitor in Table S1. There is a total of 19 cases of IL-6Rα inhibitor-related skin eruption, and 4 cases showed psoriasiform dermatitis following tocilizumab administration and no recurrence of eruption after switching into TNF inhibitor.

Although our case showed cutaneous adverse events due to sarilumab, it might be difficult to classify his skin eruption. Psoriasiform eruption was not a typical because of the histology finding. Since
pustular formation was seen in his skin biopsy specimen, palmoplantar pustulosis-like skin eruption might be a possible clinical manifestation of his skin eruption.

There have already been 4 cases of anti-IL-6R antibody tocilizumab-induced psoriasiform drug eruption.6–9 Because, IL-6 deficient mice exposed to chemicals increase cutaneous inflammatory cytokines, such as TNF and IL-1β.10 Therefore, it is speculated that these inflammatory cytokines might contribute to the development of paradoxical adverse reaction.

DECLARATION SECTION
Approval of the research protocol: No human participant was involved in this study.
Informed Consent: N/A.
Registry and the Registration No. of the study/trial: N/A.
Animal Studies: N/A.

CONFLICT OF INTEREST
The authors declare no conflict of interest.

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