

Sarilumab-induced cutaneous adverse event

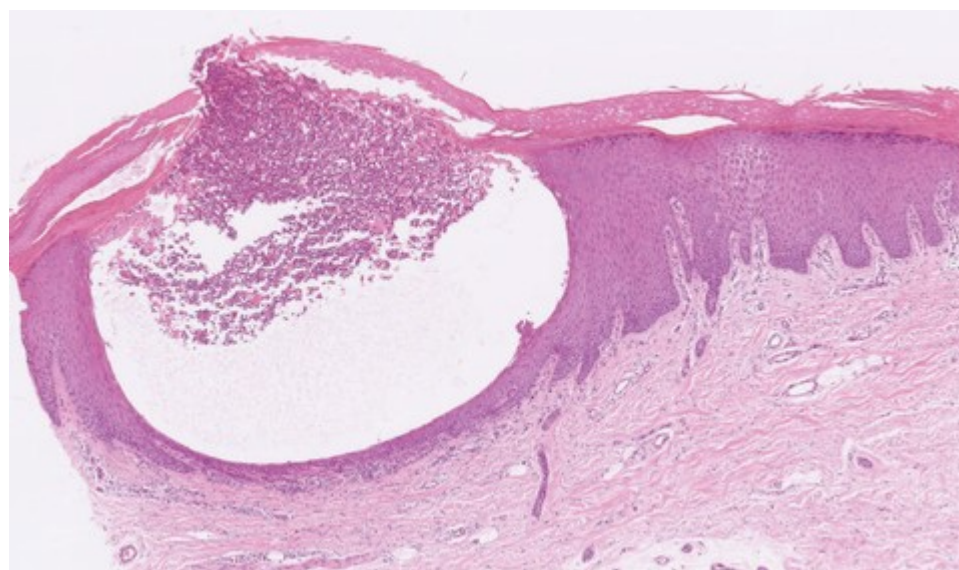
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Abstract

Histological analysis. A skin biopsy taken from his sole showed an intraepidermal pustule with hyperkeratosis



Dear Editor,

IL-6 is a representative inflammatory cytokine leading to inflammation, cell differentiation, and proliferation.¹ Therefore, the blockade of this cytokine signaling is expected to show beneficial potent in various inflammatory diseases, such as rheumatoid arthritis.¹ Although tocilizumab is a firstly available humanized monoclonal antibody against IL-6R subunit IL-6R α , sarilumab is a fully human monoclonal antibody against IL-6R α 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.²⁻⁵ 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 administered 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.

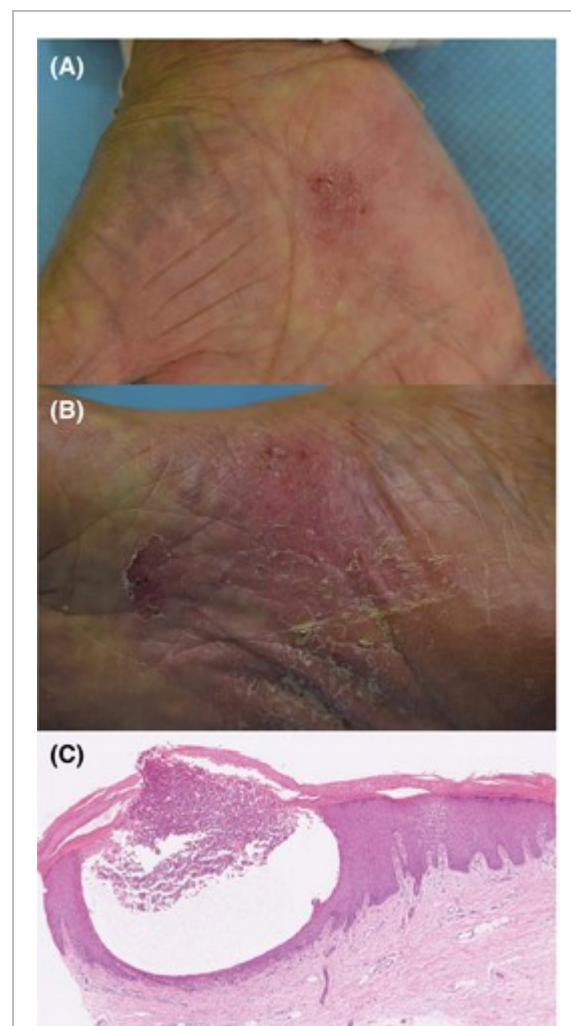


FIGURE 1

[Open in figure viewer](#) | [↓ PowerPoint](#)

Clinical manifestation and histological analysis. (A, B) Clinical appearance. Scaly erythematous plaques with pustules on (A) his hand and (B) sole. (C) Histological analysis. A skin biopsy taken from his sole showed an intraepidermal pustule with hyperkeratosis

Although this is the first case report showing a cutaneous adverse event due to sarilumab, there have already been several cases of tocilizumab-induced cutaneous drug reaction. We summarized the cases with cutaneous adverse reaction due to IL-6R α inhibitor in Table [S1](#). There is a total of 19 cases of IL-6R α 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-1 β .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.

Supporting Information



Filename	Description
cia212208-sup-0001-TableS1.docx Word document, 43.3 KB	Table S1

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Supplementary Table 1. The clinical characteristics of cutaneous adverse events by IL-6R inhibitors

Author	Age	Sex	Disease	Clinical manifestation	The causative agent	Treatment
Matsushima et al.(1)	26	Female	JIA	Psoriasiform	Tocilizumab	Tocilizumab continued Topical steroid
Palmou-Fontana et al.(2)	79	Female	RA	Psoriasiform	Tocilizumab	Tocilizumab discontinued Topical steroid Certolizumab treatment without eruption
Mori T, et al. (3)	69	Female	RA	Pustular eruption	Tocilizumab	Tocilizumab discontinued Topical steroid
Yoshiki R, et al. (4)	61	Male	RA	Multiple papules	Tocilizumab	Tocilizumab discontinued Topical steroid
Nakamura M, et al. (5)	62	Female	RA	Erythroderma	Tocilizumab	Tocilizumab discontinued Topical steroid
Fechtenbaum M (6)	34	Female	RA	Toxicoderma	Tocilizumab	No description
Wu CP, et al. (7)	67	Female	RA	cutaneous reactive endothelioma tosis	Tocilizumab	No description
Hamada K, et al. (8)	55	Female	RA	Photosensitivity	Tocilizumab	Tocilizumab discontinued Oral prednisolone (15 mg/day) Topical steroid
Ben Said B, et al. (9)	69	Female	RA	DRESS syndrome	Tocilizumab	No description
Zuelgaray E, et al. (10)	55	Female	Adult onset Still disease	DRESS syndrome	Tocilizumab	No description
Mansour Y, et al. (11)	64	Female	RA	Eruptive nevi	Tocilizumab	No description
Hayakawa M, et al. (12)	74	Male	RA	Psoriasiform	Tocilizumab	Topical steroid
Pelechas E, et al. (13)	60	Male	RA	Granuloma annulare	Tocilizumab	Tocilizumab discontinued Prednisolone (15 mg/day)

Saito Y, et al. (14)	56	Female	RA and Crohn's disease	Psoriasiform	Tocilizumab	TCZ discontinued Prednisolone (30 mg/day)
Lin CH, et al. (15)	67	Female	RA	Wolf's post-herpetic isotopic response	Tocilizumab	Tocilizumab discontinued Diphenhydramine, prednisolone
Katsuda K, et al. (16)	67	Female	anti-aquaporin-4 antibody-positive neuromyelitis optica	Granuloma annulare	Tocilizumab	Topical steroid
Inoue A, et al. (17)	68	Female	RA	Pseudolymphoma	Tocilizumab	Tocilizumab discontinued Topical steroid
Kawashiri S. (18)	34	Female	RA	Infusion reaction	Tocilizumab	No description
Our case	80	Male	RA	Palmoplantar pustulosis-like eruption	Sarilumab	Sarilumab discontinued Topical steroid Golimumab treatment without eruption

JIA: juvenile idiopathic arthritis, RA: rheumatoid arthritis, DRESS: drug reaction with eosinophilia and systemic symptoms

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