

CORRESPONDENCE

Sarilumab-induced cutaneous adverse event

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 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 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

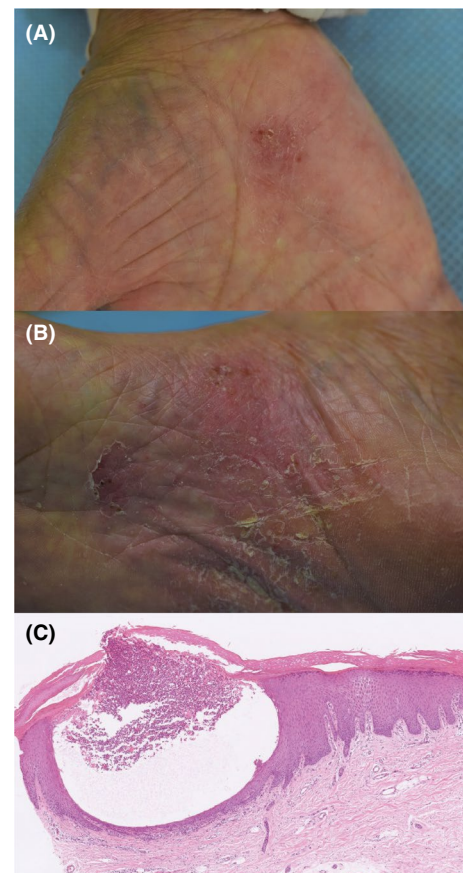


FIGURE 1 Clinical manifestation and histological analysis. (A, B) Clinical appearance. Scaly erythematous plaques with pustules on (A) his hand and (B) sole. (C) Histological analysis. A skin biopsy taken from his sole showed an intraepidermal pustule with hyperkeratosis

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

© 2021 The Authors. *Journal of Cutaneous Immunology and Allergy* published by John Wiley & Sons Australia, Ltd on behalf of The Japanese Society for Cutaneous Immunology and Allergy.



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.

Sayaka Sato

Yu Sawada

Motonobu Nakamura

Department of Dermatology, University of Occupational and Environmental Health, Kitakyushu, Japan

Correspondence

Yu Sawada, Department of Dermatology, University of Occupational and Environmental Health, 1-1, Iseigaoka, Yahatanishi-Ku, Kitakyushu, Fukuoka, 807-8555, Japan.

Email: long-ago@med.uoeh-u.ac.jp

ORCID

Yu Sawada <https://orcid.org/0000-0001-8793-708X>

REFERENCES

1. Choy EH, De Benedetti F, Takeuchi T, Hashizume M, John MR, Kishimoto T. Translating IL-6 biology into effective treatments. *Nat Rev Rheumatol*. 2020;16(6):335-45.

2. Tarkiainen M, Tynjälä P, Vähäsalo P, Lahdenne P. Occurrence of adverse events in patients with JIA receiving biologic agents: long-term follow-up in a real-life setting. *Rheumatology (Oxford)*. 2015;54(7):1170-6.
3. Inoue A, Sawada Y, Ohmori S, Omoto D, Haruyama S, Yoshioka M, et al. CD30-positive cutaneous pseudolymphoma caused by tocilizumab in a patient with rheumatoid arthritis: case report and literature review. *Acta Derm Venereol*. 2016;96(4):570-1.
4. Hamada K, Sawada Y, Yamaguchi T, Ohmori S, Omoto D, Haruyama S, et al. Photosensitivity due to tocilizumab presenting with erythema multiforme-like lesions. *Eur J Dermatol*. 2016;26(5):503-4.
5. Katsuda K, Arase N, Nakagawa Y, Tanemura A, Fujimoto M. Case of granuloma annulare after using tocilizumab. *J Dermatol*. 2020;47(4):e117-e19.
6. Matsushima Y, Hayashi A, Mizutani K, Kondo M, Nakai Y, Habe K, et al. Psoriasiform dermatitis developing during treatment of juvenile idiopathic arthritis with tocilizumab. *Case Rep Dermatol*. 2019;11(3):317-21.
7. Palmou-Fontana N, Sánchez Gaviño JA, McGonagle D, García-Martínez E, Iñiguez de Onzoño Martín L. Tocilizumab-induced psoriasiform rash in rheumatoid arthritis. *Dermatology*. 2014;228(4):311-3.
8. Hayakawa M, Izumi K, Higashida-Konishi M, Ushikubo M, Tsukamoto M, Akiya K, et al. Tocilizumab-induced psoriasis-like eruption resolved by shortening the dose interval in a patient with rheumatoid arthritis: a case-based review. *Rheumatol Int*. 2019;39(1):161-6.
9. Saito Y, Hayashi S, Gonmori T, Hamasaki Y, Igawa K. Interrupting tocilizumab therapy-induced psoriasis-like eruption in a patient with rheumatoid arthritis and Crohn's disease. *Int J Dermatol*. 2020;59(5):e159-e60.
10. Lee EG, Mickle-Kawar BM, Gallucci RM. IL-6 deficiency exacerbates skin inflammation in a murine model of irritant dermatitis. *J Immunotoxicol*. 2013;10(2):192-200.

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

How to cite this article: Sato S, Sawada Y, Nakamura M.

Sarilumab-induced cutaneous adverse event. *J Cutan Immunol Allergy*. 2022;5:67-68. <https://doi.org/10.1002/cia2.12208>