

## Paradoxical Pustular Psoriasis Following Treatment of Chronic Plaque Psoriasis with Ustekinumab

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### Abstract

A 51-year-old female with red plaques and scales for 20 years, aggravated with pustules for more than 10 days. Physical examination: scattered red patches, silver-white scales, thin film, Auspitz sign (+) can be seen on the head and face. The trunk and limbs were scattered in large erythema and erythema, on which were dense pustules of the size of chestnut. The central color of local pustules was brown, presenting target-shaped lesions, and some pustules fused into pus lake. Vulvar mucosa scattered in pustules, erosion surface. Nail clipping thimble changes, deck thickening changes. Histopathology: Hyperkeratosis, fusion keratosis, thinning or disappearance of granular layer, epidermal psoriatic hyperplasia, munro and Kogoj microabscess, dermal papilloma, vascular dilatation, perivascular lymphocyte infiltration. Diagnosis: pustular psoriasis.

**Keywords:** Ustekinumab, IL-12/IL-23, Pustular Psoriasis

The patient was a 51-year-old female with a 20-year history of plaque psoriasis. The lesions mainly manifested as large erythema and red plaques on the trunk and limbs, with silver white scales attached to them. Used methotrexate, avitamin A treatment, treatment effect is not good. After completing the relevant screening in September 2019 and showing no obvious contraindications, the patient was given Ustekinumab 45mg subcutaneous injection, which was given at the 4th week respectively according to the instructions, and every 12 weeks thereafter. During the treatment, the whole body rash subsided significantly and no obvious discomfort was observed. More than 10 days ago, the patient's trunk reappeared erythema scales, rash increased rapidly, involving the whole body, and a large number of pustules appeared, which fused into pus lake, accompanied by fever, with the temperature up to 37.4°C. Physical examination: scattered red patches, silvery white scales, thin film, Auspitz sign (+) were observed on the head and face. The trunk and limbs were scattered in large erythema and erythema, on which were dense pustules of the size of chestnut. The central color of local pustules was brown, presenting target-shaped lesions, and some pustules fused into pus lake. Vulvar mucosa scattered in pustules, erosion surface. Nail clipping thimble changes, deck thickening changes. Laboratory examination: the absolute value of neutrophils was  $6.34 \times 10^9/L$ . IgE quantitative: 255.5IU/mL; Blood sedimentation: 52 mm/h. CRP: 53.76 mg/L. Smear test of general bacteria in pus: very small amount of gram-positive cocci; Bacterial culture + drug sensitivity test: No bacterial growth was observed. No obvious abnormalities were found in residual calcitonin, immune penta, electrolyte penta, liver function penta,

kidney function penta, blood lipid, urine routine, stool routine and ANA quantitative analysis. Pathological biopsy of lesions on the back showed hyperkeratosis, fusion keratosis, thinning or disappearance of granular layer, epidermal psoriatic hyperplasia, munro and Kogoj microabscess, dermal papilloma, vascular dilatation, perivascular lymphocyte infiltration. Diagnosis: pustular psoriasis. Considering that Ustekinumab induced the patients to change from plaque psoriasis to pustular psoriasis, we stopped the treatment with Ustekinumab, and the rash subsided within 3 days after local corticosteroid treatment and Ixekizumab treatment.

Ustekinumab is a whole-human monoclonal antibody directed against the p40 subunit common to IL-12 and IL-23, and is generally administered subcutaneously. IL-12 and IL-23 have been confirmed to be closely related to the occurrence and development of psoriasis [1]. IL-23 is a pro-inflammatory cytokine composed of two subunits, P19 and P40. The P40 subunit is shared with IL-12. IL-23 and IL-12 have different receptors and different roles. IL-12 induces the development of Th1 cells to produce interferon, while IL-23 is involved in the differentiation of Th17 cells in the presence of proinflammatory action, especially TGF- $\beta$  and IL-6. Activated Th17 cells produced IL-17A, IL-17F, IL-6, IL-22, TNF- $\alpha$ , and GM-CSF. Ustekinumab blocks the Th1 and Th17 inflammatory pathways by blocking IL-12 and IL-23 binding interactions with their receptors [2]. Ustekinumab has been proven to be an effective and safe treatment for moderate to severe plaque psoriasis and is recommended by the guidelines as an IL12/23P40 inhibitor for the treatment of moderate

to severe plaque psoriasis and psoriatic arthritis [2]. The most common adverse reactions of Ustekinumab include nasopharyngitis, upper respiratory tract infection, headache, and injection site reactions [3, 4]. However, in recent years, with the increase of clinical use, other adverse reactions are also increasing, such as the induction of pustular psoriasis [5].

Ustekinumab is a highly targeted drug for psoriasis, with few side effects. It has been reported that 5 cases of plaque psoriasis were induced to transform into pustular psoriasis, or were induced to develop pustular psoriasis. The first case was reported in 2011 in a Greek patient with plaque psoriasis who developed pustular psoriasis after treatment with Ustekinumab [6]. In the second case, the patient developed pustular psoriasis 4 days after each injection of Ustekinumab, and disappeared after withdrawal of the drug [7]. In the third case, a 47-year-old patient with psoriasis developed pustular psoriasis after treatment, which completely disappeared after the replacement of Ustekinumab with adamumab [8]. Caca-biljanovska et al. reported the appearance of pustular psoriasis 10 weeks after the introduction of Ustekinumab in a 34-year-old patient with psoriasis, and the pustules disappeared only after topical steroid use [9]. In the fifth case, a 30-year-old patient with psoriasis was treated with Ustekinuma instead of Infliximab, and developed pustular psoriasis 2 weeks after the second injection of Ustekinumab [10]. A review of relevant literature found that infliximab has also been reported to induce pustular psoriasis [11]. Antitumor necrosis factor-induced psoriasis may be caused by a decrease in TNF- $\alpha$  and an increase in production of plasma cell-like dendritic cell interferon - A (IFN- A).IFN- A can indirectly promote the activation of T cells through the activation of myeloid dendritic cells, or directly promote the activation of T cells through IFN-A sensitive T cells, so that T cells can accumulate locally in the skin and cause local psoriatic changes [12]. It is reasonably speculated that Ustekinumab can reduce IL-23 and Th17 cell-induced TNF- $\alpha$  levels, thereby increasing IFN- A, leading to pustular psoriasis. These reactions to biological agents that contradict the purpose of treatment should be of concern to physicians.

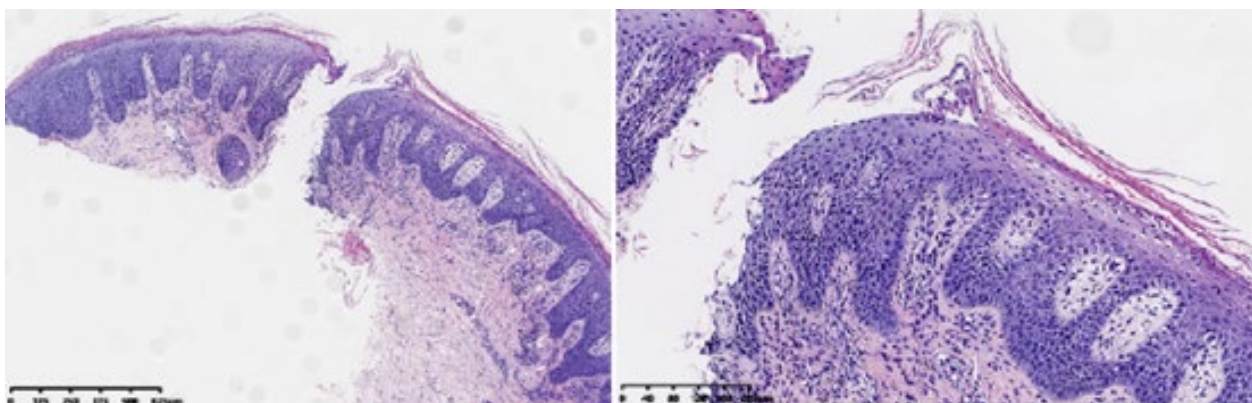
This is a case of pustular psoriasis induced by Ustekinumab, which responded to Ixekizumab therapy.



Before treatment: the trunk and limbs were scattered in large erythema and erythema, on which were dense pustules about the size of a chestnut. The central color of local pustules was brown, presenting target-shaped lesions, and some pustules fused into pus lake



After treatment: whole body skin loss basically subside.



Pathology: Hyperkeratosis, fusion keratosis, granular layer thinning or disappearance, epidermal psoriatic hyperplasia, munro and Kogoj microabscess, dermal papilloma, vascular dilatation, perivascular lymphocyte infiltration.

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## References

1. Elliott, M., Benson, J., Blank, M., Brodmerkel, C., Baker, D., Sharples, K. R., & Szapary, P. (2009). Ustekinumab: lessons learned from targeting interleukin-12/23p40 in immune-mediated diseases. *Annals of the New York Academy of Sciences*, 1182(1), 97-110.
2. Teng, M. W., Bowman, E. P., McElwee, J. J., Smyth, M. J., Casanova, J. L., Cooper, A. M., & Cua, D. J. (2015). IL-12 and IL-23 cytokines: from discovery to targeted therapies for immune-mediated inflammatory diseases. *Nature medicine*, 21(7), 719-729.
3. López-Ferrer, A., Laiz, A., & Puig, L. (2017). The safety of ustekinumab for the treatment of psoriatic arthritis. *Expert Opinion on Drug Safety*, 16(6), 733-742.
4. US FDA. Tremfya® (guselkumab): US prescribing information (2017) <https://www.accessdata.fda.gov/>. Accessed 23 Oct 2018.
5. Benzaquen, M., Flachaire, B., Rouby, F., Berbis, P., & Guis, S. (2018). Paradoxical pustular psoriasis induced by ustekinumab in a patient with Crohn's disease-associated spondyloarthropathy. *Rheumatology international*, 38(7), 1297-1299.
6. Gregoriou, S., Kazakos, C., Christofidou, E., Kontochristo-Poulos, G., Vakis, G., & Rigopoulos, D. (2011). Pustular psoriasis development after initial ustekinumab administration in chronic plaque psoriasis. *EJD. European journal of dermatology*, 21(1), 104-105.
7. Wenk, K. S., Claros, J. M., & Ehrlich, A. (2012). Flare of pustular psoriasis after initiating ustekinumab therapy. *Journal of dermatological treatment*, 23(3), 212-214.
8. Hay, R. A. S., & Pan, J. Y. (2014). Paradoxical flare of pustular psoriasis triggered by ustekinumab, which responded to adalimumab therapy. *Clinical and Experimental Dermatology*, 39(6), 751-752.
9. Caca-Biljanovska, N., V'lickova-Laskoska, M., & Laskoski, D. (2013). Successful management of ustekinumab-induced pustular psoriasis without therapy discontinuation. *Acta Dermatovenerologica Croatica*, 21(3), 202-202.
10. Suh, H. Y., Ahn, J. Y., Park, M. Y., & Youn, J. I. (2018). Exacerbation of infliximab-induced paradoxical psoriasis after ustekinumab therapy. *The Journal of dermatology*, 45(3), 332-333.
11. Shimokata, M., Namiki, T., Tokoro, S., Ugajin, T., Miura, K., & Yokozeki, H. (2018). Case of psoriasiform and pustular eruptions in addition to alopecia as a paradoxical reaction induced by infliximab. *The Journal of Dermatology*, 45(12), e331-e333.
12. Ciccarelli, F., De Martinis, M., Sirufo, M. M., & Ginaldi, L. (2016). Psoriasis induced by anti-tumor necrosis factor alpha agents: a comprehensive review of the literature. *Acta Dermatovenerologica Croatica*, 24(3), 169-169.

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