Successful treatment of generalized pustular psoriasis with secukinumab: a report of two cases

Zhi-Lin Sun, Zi-Lian Liu, Yuan-Yuan Xu, Xiu-Lian Zhang, Chun-Lei Zhang, Xin Guan

Department of Dermatology, Peking University Third Hospital, Beijing 100191, China.

To the Editor: Generalized pustular psoriasis (GPP) is a rare and severe form of psoriasis for which traditional treatment approaches may not be effective. The traditional approach is systemic treatment with acitretin, methotrexate, and cyclosporin; however, obvious side effects often occur during drug administration, limiting their clinical application. Secukinumab, a fully human anti-interleukin (IL)-17A monoclonal antibody, demonstrates efficacy in treating moderate to severe plaque-type psoriasis. Nonetheless, there are limited evidence-based real-world data on GPP treatment with secukinumab. Two cases of GPP were successfully treated with secukinumab in Peking University Third Hospital recently. This study was approved by the Ethics Committee of our hospital (No. 328-01).

A 21-year-old Chinese man with a 4-month history of plaque-type psoriasis experienced a sudden exacerbation after a flu-like episode. He developed a generalized pustular eruption, which affected 86% of the body surface area (BSA), associated with high fever (up to 41°C) and itching. On examination, he had disseminated, partly confluent lakes of pustules primarily over the trunk as well as the upper and lower extremities, with pitting edema on his face and lower legs [Figure 1A]. His psoriasis area and severity index (PASI) was 32.5 and the dermatology life quality index (DLQI) was 15 on admission. The laboratory findings on admission revealed neutrophilic leukocytosis, with a white blood cell count of 9.86×10^9/L (reference range, 3.5–9.5×10^9/L), neutrophil count of 8.09×10^9/L (reference range, 1.8–6.3×10^9/L), and C-reactive protein (CRP) level of 7.7 mg/dL (reference range, ≤0.8 mg/dL), as well as increased levels of liver enzymes and CRP. Thus, he received a diagnosis of GPP.

Treatment with secukinumab, the recently approved drug for plaque psoriasis (also called psoriasis vulgaris), was initiated. The patient received the standard regimen: 300 mg subcutaneously once weekly at weeks 0–4, followed by 300 mg every four weeks. Within 8 h after the first dose, defervescence occurred (down to 36.5°C) and his general state improved; partial resolution of pustules, with marked reduction in erythema was observed after 48 h [Figure 1B]. After the second dose of secukinumab, PASI-75 was achieved [Figure 1C]. PASI-90 was achieved at week 6 and complete remission was observed at week 8, with DLQI of 0, which was further maintained until week 11.

A 16-year-old Chinese girl with plaque-type psoriasis since the age of 10 years suddenly developed GPP for seven days with no obvious cause (PASI: 37.8, 42% of BSA) [Figure 1D]. She was afebrile and her DLQI was 17. Her laboratory findings showed no obvious abnormality.

The patient received the standard regimen of secukinumab: 300 mg subcutaneously once weekly at weeks 0–4, followed by 300 mg every four weeks. Within 4 days after the first dose, the pustules resolved. After the first week of secukinumab treatment, PASI75 was achieved. Complete remission was achieved at week 8, with DLQI of 0 [Figure 1E], which was further maintained until week 24.

Recent research suggests that the pathogenesis of GPP is closely related to the recruitment of neutrophils and other inflammatory cells in the epidermis via binding to IL-36 and IL-36 receptor (IL-36R). IL-36 receptor antagonist (IL-36RA) encoded by the IL-36RN gene can block the pro-inflammatory signaling pathway by preventing IL-36 from binding to its receptor. In addition, activation of the tumor necrosis factor (TNF)-α/IL-17/IL-22 axis can accelerate and aggravate this reaction, and the interaction between the IL-36 axis and TNF-α/IL-17/IL-22 axis leads to GPP.[1] IL-17, as an indispensable link, plays a very important role in the development of plaque psoriasis and GPP.

In a 52-week open-label phase 3 study in Japanese patients, 10 of 12 patients with generalized pustular psoriasis (83%) were rated as "very much improved" or "much improved" on the overall clinical efficacy scale at week 16.[2] Most patients experienced the greatest improvement within 3 weeks, and

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Correspondence to: Dr. Xin Guan, Department of Dermatology, Peking University Third Hospital, 49 North Garden Road, Haidian District, Beijing 100191, China
E-Mail: guanxin1@sina.com

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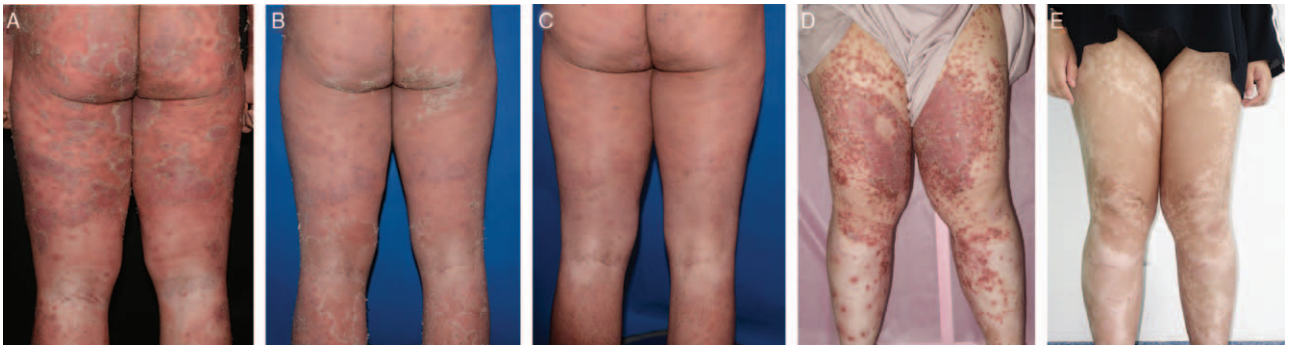

Figure 1: (A) Clinical images of case 1 of the lower limbs and hip before treatment. (B) 2 days after the first injection of Secukinumab. (C) 1 day after the second dose. (D) Clinical images of case 2 of the Lower limbs before treatment. (E) 8 week after the first injection of Secukinumab.

some patients achieved complete remission at week 12. Wilsmann-Theis *et al*[3] reported for the first time the successful treatment of GPP with secukinumab in five adult patients without IL-36RN mutation. Ho *et al*[4] reported the first successful treatment of refractory juvenile GPP with secukinumab in a 6-year-old boy with IL-36RN mutation. A recent study reported that secukinumab is effective for GPP patients with IL-36RN mutations and its efficacy is not affected by the type of mutation.[5] The above findings of studies showed that secukinumab had good efficacy for all types of GPP.

In this study, the male patient was suspected to be a new and rapidly progressing pustular psoriasis, while the girl had a history of psoriasis vulgaris for many years and developed pustular psoriasis without any obvious inducement. The two patients in our study had not received standard systemic treatment previously and achieved complete remission at week 8. However, in the previous studies, almost all patients treated with secukinumab had failed prior therapy, including corticosteroids, acitretin, cyclosporin A, or any other biologics, and they achieved complete remission (12 weeks) later than the patients in our report did (8 weeks).

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the article. The patients understand that their name and initials will not be published and due efforts will be made to conceal the identity of the patients, although anonymity cannot be guaranteed.

Conflicts of interest

None.

References

1. Furue K, Yamamura K, Tsuji G, Mitoma C, Uchi H, Nakahara T, *et al*. Highlighting interleukin-36 signalling in plaque psoriasis and pustular psoriasis. Acta Derm Venereol 2018;98:5–13. doi: 10.2340/00015555-2808.
2. Imafuku S, Honma M, Okubo Y, Komine M, Ohtsuki M, Moritaet A, *et al*. Efficacy and safety of secukinumab in patients with generalized pustular psoriasis: a 52-week analysis from phase III open-label multicenter Japanese study. J Dermatol 2016;43:1011–1017. doi: 10.1111/1346-8138.13306.
3. Wilsmann-Theis D, Schnell ML, Ralser-Isselstein V, Bieber T, Schön MP, Hüffmeier U, *et al*. Successful treatment with interleukin-17A antagonists of generalized pustular psoriasis in patients without IL36RN mutations. J Dermatol 2018;45:850–854. doi: 10.1111/1346-8138.14318.
4. Ho PH, Tsai TF. Successful treatment of refractory juvenile generalized pustular psoriasis with Secukinumab monotherapy: a case report and review of published work. J Dermatol 2018;45:1353–1356. doi: 10.1111/1346-8138.14636.
5. Gabeff R, Safar R, Leducq S, Maruani A, Sarrabay G, Touitou I, *et al*. Successful therapy with secukinumab in a patient with generalized pustular psoriasis carrying homozygous IL36RN p.His32Arg Mutation. Int J Dermatol 2019;58:e16–e17. doi: 10.1111/ijd.14293.

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