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CORRESPONDENCE

The utility of *IL36RN* mutation analysis in an elderly patient with generalized pustular psoriasis patient treated with secukinumab

Generalized pustular psoriasis (GPP) is characterized by acute flare-ups induced by various factors[1] but few reports have described GPP onset or flare-ups induced by coronavirus disease 2019 (COVID-19). We present a case of GPP that presented with SARS-CoV-2 infection under the control of secukinumab.

A 22-year-old woman presented with erythema and pustules on her trunk with fever during her second pregnancy. She had no history or family history of GPP or psoriasis vulgaris at that time. She had not taken any new medications before the eruptions developed. We diagnosed the patient with impetigo herpetiformis (IH).

When she was 45 years old, we diagnosed the patient with GPP after a second flare-up induced by fever. When she was 59 years old, the third flare-up occurred after 7 days of oral nonsteroidal anti-inflammatory drug therapy. She had been managed with oral etretinate and a topical steroid.

After 3 months, she stopped oral etretinate because of the alopecia, then the fourth flare-up occurred. Physical examination revealed erythema and pustules on her trunk and limbs (Figure 1A,B). Skin biopsy revealed Kogoj's spongiform pustules in the epidermis (Figure 1C). A heterogeneous c.28C>T (p.Arg10X) mutation in *IL36RN* gene coding interleukin (IL) 36 receptor antagonist was revealed (Figure 1D). The erythema partially resolved with the addition of cyclosporine. Secukinumab was started after a 27-year history of GPP. Subsequently, the patient has maintained complete remission by secukinumab 300 mg every 4 weeks for 6 years (Figure 1E,F).

When she was 65 years old, she was diagnosed with COVID-19 with new-onset fever, fatigue, cough, and sputum. Her clinical course of COVID-19 was mild and had no effect on GPP. We restarted secukinumab 4 weeks later from the day of positive with the antigen examination kit for COVID-19.

Impetigo herpetiformis is a variant of GPP that develops during pregnancy.[2] GPP is associated with mutations in *IL36RN*.[2] Among 10 IH patients of East Asian reported together with the results of genetic analyses, 7 had *IL36RN* mutations.[2] All were founder mutations causing GPP in East Asia: c.28C>T (p.Arg10X) or c.115 + 6T>C (p.Arg10ArgfsX1).[2]

In one study comparing treatments for GPP, in-hospital mortality was lower in the biologics group (1.0%) than in the oral-agents group (3.7%) and the corticosteroids-only group (9.1%) ($p < .001$). Morbidity followed the same pattern: 5.4% versus 8.2% versus 12%, respectively ($p = .02$).[3] Among patients who received biologics, IL-17 inhibitor use increased over time, with in-hospital mortality and morbidity comparable to those of patients taking tumor necrosis factor inhibitors.[3] IL-17 is associated with the hyper-inflammatory state in COVID-19; therefore, IL-17 inhibitors are promising targets for the prevention of aberrant inflammation and acute respiratory distress in COVID-19.[4]

A retrospective analysis of 10 patients with psoriasis who developed COVID-19 during treatment with biologics showed that none developed severe symptoms. Six patients developed moderate symptoms, and 4 mild developed symptoms.[5]

The *IL36RN* mutation status might help predict postpartum flare-ups in patients with GPP. The mutation analyses are useful for GPP women to enable preparation for biologic therapy to treat intractable flare-ups.

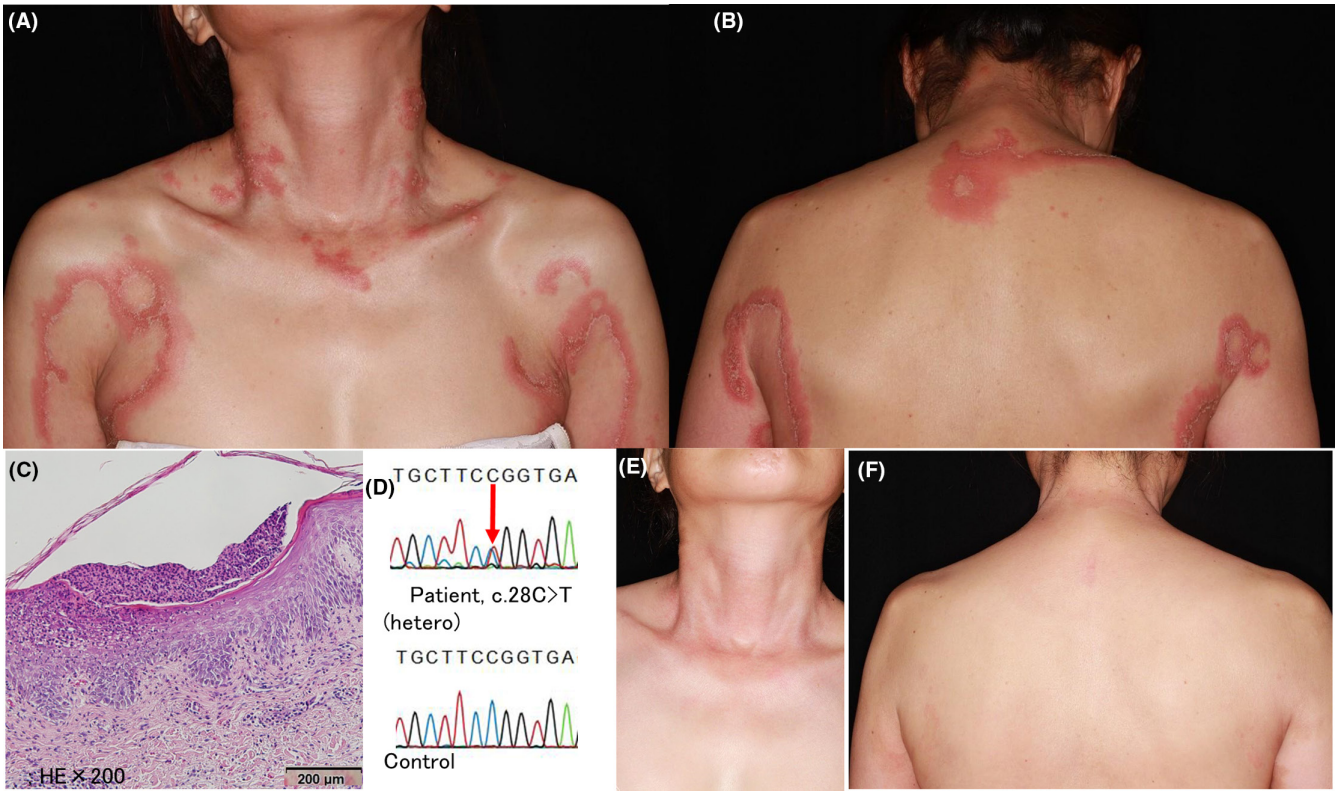

FIGURE 1 Clinical and histological features. (A, B) Multiple, annular, erythematous lesions with pustules were observed on the trunk and extremities before secukinumab therapy. (C) Histological examination shows a Kogoj's spongiform pustule (hematoxylin–eosin (HE) staining, original magnification ×200). (D) Mutational analysis of *IL36RN*. Direct sequence analysis revealed a heterogeneous c.28C>T (p.Arg10X) mutation in *IL36RN* in the patient's genomic DNA. (E, F) The erythema and pustules decreased after secukinumab therapy.

KEYWORDS

biologic drugs, GPP, impetigo herpetiformis, interleukin-17, severe acute respiratory syndrome-coronavirus-2

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest. Management of the peer-review process, and all editorial decision-making, for this article was undertaken by Editor in Chief, Prof. Manabu Fujimoto.

ETHICS STATEMENT

Approval of the research protocol: The protocol for this research project has been approved by a suitably constituted Ethics Committee of the institution and it conforms to the provisions of the Declaration of Helsinki. The study protocol was approved by the Committee of Medical Ethics of Fujita Health University School of Medicine. Approval No. HG20-049.

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