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LETTER TO THE EDITOR

Flare-up of generalized pustular psoriasis following Pfizer-BioNTech BNT162b2 mRNA COVID-19 vaccine: Two cases without mutations of *IL36RN* and *CARD14* genes

Dear Editor,

Generalized pustular psoriasis (GPP) is an inflammatory disease characterized by an acute generalized eruption with small sterile pustules, accompanied by systemic symptoms. Most GPP patients without preceding psoriasis vulgaris (PsV) have mutations in the gene interleukin 36 receptor antagonist (*IL36RN*).[1] GPP is triggered by several factors including infections, pregnancy, and corticosteroids. We report two cases of GPP induced by the Pfizer-BioNTech BNT162b2 mRNA coronavirus disease 2019 (COVID-19) vaccine.

Case 1 was a 60-year-old woman who was admitted due to fatigue and diffuse erythema 8 days after the second dose of Pfizer mRNA COVID-19 vaccine. She was diagnosed with impetigo herpetiformis during her second pregnancy at 30 years old. She relapsed only once when she was 47 years old, and oral etretinate had been effective; she had been in remission for 13 years. Physical examination revealed high fever (39.4°C) and generalized annular erythema with scales and pustules on the neck, trunk, and extremities (Figure 1a–c). Laboratory findings showed elevated white blood cells (WBC; 12 020/μL) and serum C-reactive protein (CRP; 6.34 mg/dL). The COVID-19 polymerase chain reaction (PCR) test and bacterial cultures of the blood and pustules were all negative. A biopsy specimen from a pustule showed a collection of numerous neutrophils within the upper stratum spinosum, forming spongiform pustules of Kogoj (Figure 1d). Oral etretinate (30 mg/day) was reintroduced, and the skin rash improved in 1 week.

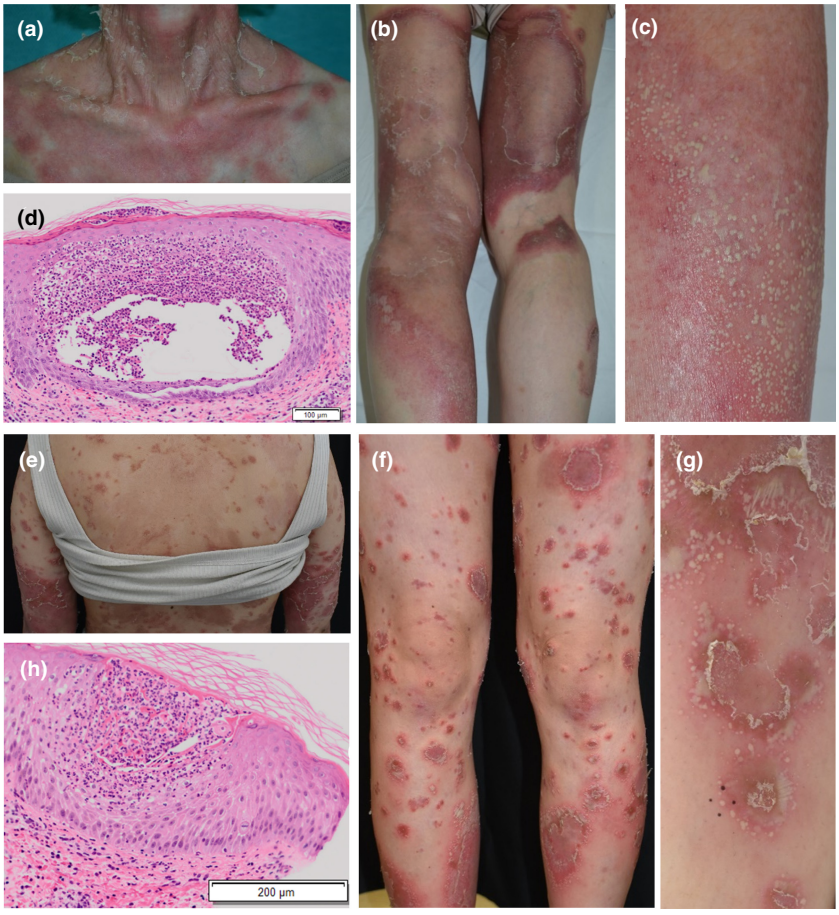

FIGURE 1 (a–d) Case 1. (a) Fresh erythematous macules with scales on the neck. (b,c) Large annular erythematous macules with sterile pustules and scales on the legs. (d) Histological examination displaying intracorneal pustule and infiltration of numerous neutrophils in the epidermis, forming spongiform pustules of Kogoj (hematoxylin–eosin [HE]; scale bar, 100 μm). (e–h) Case 2. (e) Diffuse scaly erythema on the trunk. (f,g) Fresh and annular erythema with small sterile pustules and scales on the edematous lower legs. (h) Intraepidermal pustules with spongiform pustules of Kogoj (HE; scale bar, 200 μm).

Case 2 was an 18-year-old woman who was admitted with high fever and skin rash 7 days after the first Pfizer mRNA COVID-19 vaccine dose. Her mother had PsV. The patient was diagnosed with PsV at 5 years old. She had been treated with calcipotriol hydrate/betamethasone dipropionate ointment. The skin rash was generalized with pustules on the face, trunk, and extremities (Figure 1e–g). Laboratory findings showed WBC at 15 320/μL, serum CRP at 2.21 mg/dL, and interleukin (IL)-6 at 28.8 pg/mL (normal, 0–7.0). The COVID-PCR test and bacterial culture were negative. A biopsy specimen from the pustule showed Kogoj's spongiform pustule (Figure 1h).

She was first treated with cyclosporine 200 mg/day (4 mg/kg). Because the skin lesions were smoldering, secukinumab was introduced, resulting in a favorable outcome. A second vaccination dose was not administered.

In both patients, a sequencing analysis of genomic DNA derived from peripheral blood revealed no gene mutations in entire coding regions of *IL36RN* and exons 2–4 of caspase recruitment domain family member 14 (*CARD14*).

There are six reported cases of GPP following COVID-19 vaccination, including our patients.[2–5] The preceding types of psoriasis were PsV[2,4] in three cases, GPP[5] in two cases, and de novo GPP in one case.[3] The present report of GPP following vaccination in which mutation analyses were performed appears to be the first. Although we could not clarify genetic characteristics, there may be undetectable disease-related mutations because case 1 had a history of GPP without PsV and case 2 had juvenile-onset PsV with a family history. The vaccination may have triggered the GPP flares. Identifying patients who are vulnerable to the development of GPP after vaccinations is important.

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CONFLICT OF INTEREST

None declared.

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