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SHORT REPORT

Generalized erythrodermic psoriasis triggered by vaccination against severe acute respiratory syndrome Coronavirus 2

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Abstract

Generalized erythrodermic psoriasis (GEP) is a rare and potentially life-threatening variant of psoriasis. Possible triggers that have been identified to date include poorly controlled psoriasis, medications, abrupt discontinuation of anti-psoriatic treatment, and underlying systemic illnesses. However, vaccines have rarely been reported to exacerbate GEP. Herein, we report two unique cases with GEP exacerbated following a dose of the BNT162b2 mRNA vaccine for COVID-19 (as their second dose, the first being the mRNA-1273 vaccine). Based on our observations and a literature review, vaccination was considered the most likely trigger of GEP due to the close temporal relationship between the second vaccination and the onset of GEP.

KEYWORDS
BNT162b2 vaccine, COVID-19, generalized erythrodermic psoriasis, mRNA-1273 vaccine, SARS-CoV-2 vaccination

1 | INTRODUCTION

Generalized erythrodermic psoriasis (GEP) is a rare and potentially life-threatening variant of psoriasis. Possible triggers include poorly controlled psoriasis, medications, abrupt discontinuation of anti-psoriatic treatment, and underlying systemic illnesses.[1] However, vaccines have rarely been reported to exacerbate GEP. During the Coronavirus disease 2019 (COVID-19) pandemic, the US Food and Drug Administration granted emergency authorization to the mRNA-1273 vaccine for use in patients with COVID-19. Furthermore, in 2021, the BNT162b2 mRNA vaccine became the first to receive a full approval for use against COVID-19. Herein, we report two unique cases in which GEP exacerbated following a second dose with the BNT162b2 mRNA vaccine (the mRNA-1273 vaccine was administered as the first dose).

2 | CASE REPORT

This study was approved by the Research Ethics Committee of Ho Chi Minh City Hospital of Dermato-Venereology. Informed consent was obtained from the patients for participation in the study and publication of the case report.

2.1 | Case 1

A 30-year-old female patient, with a 15-year history of chronic plaque psoriasis and no comorbidities, presented to us with a generalized erythrodermic condition. Three years ago, the patient had experienced a severe, exacerbated episode in which the psoriasis area and severity index (PASI) increased to over 30 points. However, the disease was well-controlled after a 2-year course of secukinumab. Due to financial issues, our patient discontinued the treatment and opted self-treatment with traditional herbal remedies, topical corticosteroids, and vitamin-D analogs. During this period, only a few psoriatic plaques were noted on her feet and scalp (PASI <10).

Two months prior to the most recent presentation, the patient received the mRNA-1273 vaccine and experienced no adverse effects from it. However, 2 months later, after receiving the BNT162b2 vaccine as the second dose, the patient experienced pain at the injection site and developed fever (38°C), headache, and malaise that lasted for 48 h. One week later, the patient presented to us with a generalized erythrodermic condition. During this period, the patient decided to pause all anti-psoriatic treatments due to fear of adverse drug-vaccine interactions. At examination, the patient appeared fatigued and had

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fever, malaise, and poor oral intake lasting for several days. Generalized erythematous patches with marked desquamation were also noted (Figure 1).

Blood laboratory test results were normal, except for an indication of severe hypocalcemia and a mildly elevated eosinophil count. Analysis of a skin biopsy sample collected from the patient's right arm revealed regular psoriasiform epidermal hyperplasia with loss of the granular cell layer as well as neutrophils in the upper layers of the overlying parakeratotic scale. These findings were consistent with GEP (Figure S1). Following 2 weeks of treatment with acitretin (25 mg/day), the skin lesions became less erythematous and scaly.

2.2 | Case 2

The second case was a 45-year-old woman suffering from moderate stable plaque psoriasis with PASI score of 10 for more than 20 years. She was being treated with topical corticosteroids and calcipotriol and refused systemic treatments due to fear of adverse side effects. She received mixed vaccination with the mRNA-1273 vaccine as the first dose and the BNT162b2 vaccine as the second dose. The patient presented to us with diffuse erythema 1 week after the second vaccine dose (Figure 1). On clinical examination, the skin was diffusely erythematous and scaly, with involvement of 90% BSA; marked edema of lower extremities was also noted. Blood laboratory tests

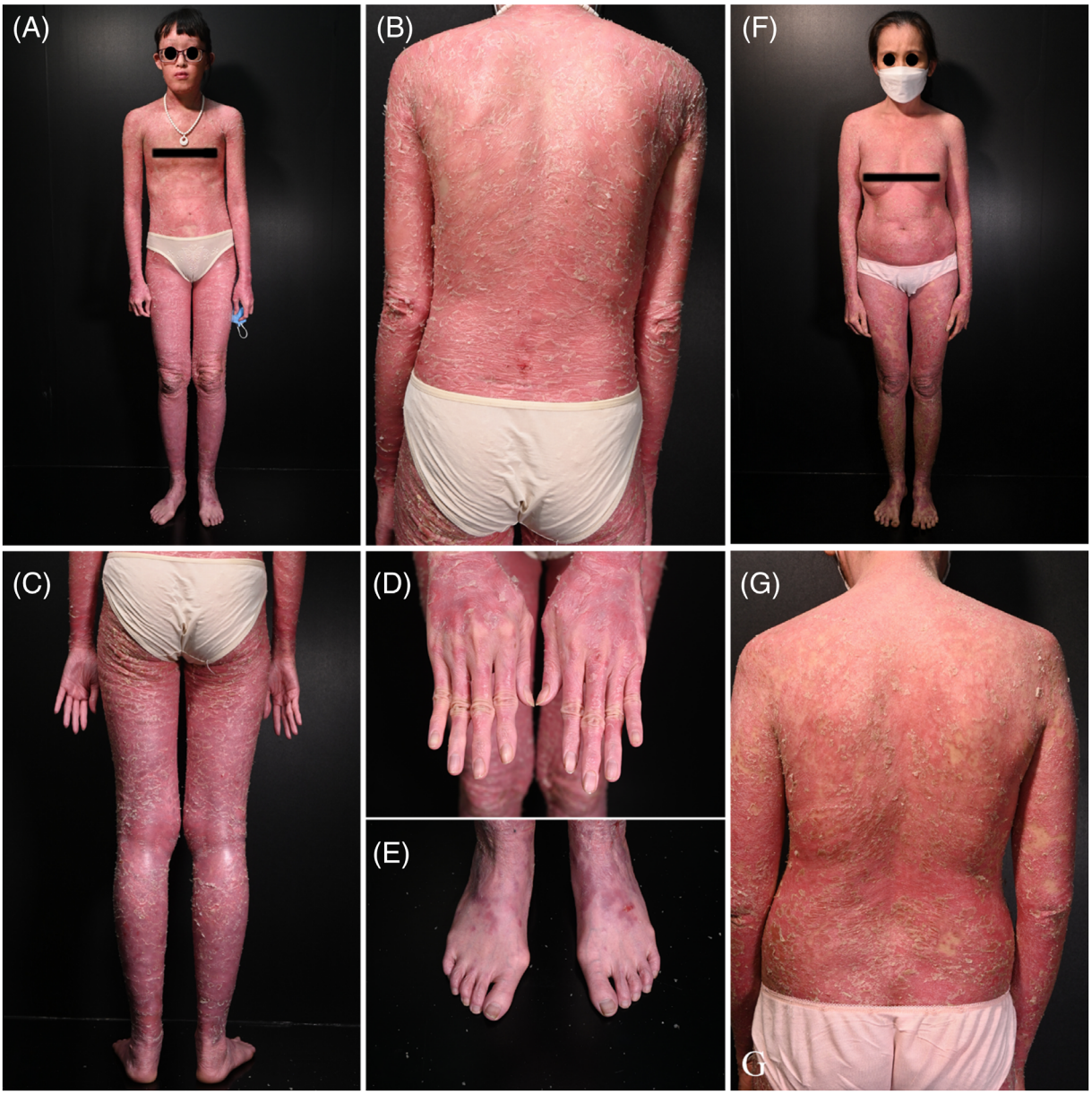

FIGURE 1 (A–C) Generalized erythroderma and exudative desquamation on the head, trunk, and extremities in combination with lower extremity edema; (D, E) Nail changes, including nail pitting and oil spots, are observed in the nails of both hands and feet (patient 1). (F, G) Generalized erythroderma affected more than 90% body surface area (patient 2)

were in a normal range. Although the patient refused a skin biopsy procedure, her medical history and clinical findings were characteristic of GEP.

3 | DISCUSSION

Psoriasis is a chronic inflammatory skin condition with several clinical subtypes, including chronic plaque psoriasis, nail psoriasis, guttate psoriasis, GEP, and pustular psoriasis. It is characterized by prominent generalized erythema and scaling of more than 75% of the body surface area.[2] Although several triggers for GEP exacerbation have been identified, vaccines have rarely been implicated as a trigger. Our first patient had consumed herbal remedies for more than a year to treat her psoriasis; however, she discontinued all treatments upon receiving the first vaccine dose due to fear of adverse drug interactions. Her psoriasis remained stable until the second dose, after which she experienced headache, fever with skin desquamation, and extensive erythema over >75% of the body surface area. We cannot completely exclude the possibility that psoriasis flare-up may be contributed from cessation of anti-psoriatic treatments. However, COVID-19 vaccination may have played a more important role because the patient experienced GEP exacerbation relatively soon (7 days) after the second vaccine dose. Similarly, in the second patient, close temporal relationship between the second vaccine dose and her GEP as well as the fact that she did not use any systemic medications suggests the second dose of vaccine was the most likely culprit for her worsening condition.

According to literature, exacerbated psoriasis is quite rare. A registry-based study by McMahon identified this phenomenon in only 2 out of 414 patients.[3] To the best of our knowledge, ours is the first report describing the occurrence of GEP after mixed vaccination with the mRNA-1273 vaccine as the first dose and the BNT162b2 vaccine as the second dose. Exacerbation of preexisting plaque psoriasis has been reported by several authors; in these reports, most patients either received topical therapy or no treatment, except for 1 patient who was on deucravacitinib for 21 months (Table 1). Furthermore, 2 cases of acute generalized pustular psoriasis, related to ChAdOx1 nCoV-19 and BNT162b2 vaccination, have also been reported.[4,5]

The mechanisms underlying the exacerbation of GEP after vaccination with the mRNA vaccines for COVID-19 are not yet understood. Unlike the pathogenesis of psoriasis vulgaris (PV), in which Th17 and Th1 activation plays a central role, the pathogenesis of GEP is largely unknown; however, it is thought to differ from that of PV. Serum immunoglobulin E levels were found to be significantly higher in patients with GEP than in patients with PV; this was attributed to Th2 differentiation. Furthermore, another study found higher interleukin (IL)-4 and IL-10 levels and an increased Th2 response in 16 patients with GEP as compared to in patients with PV and in healthy participants.[9] Previous studies on the diphtheria and Bacillus Calmette–Guérin vaccines, both mRNA vaccines, demonstrated the production of IL-6. Thus, the recruitment of Th17 cells may play a key

TABLE 1 Current literature on the exacerbation of psoriasis after vaccination against COVID-19

Authors	No. of pts	Vaccine type	Dose	Days	Pre-existing psoriasis subtype	Pre-vaccination psoriatic treatment	Type of reaction	Treatment
Krajewski et al[6]	1	Pfizer	2	5	Plaque psoriasis	Deucravacitinib	Exacerbation of pre-existing plaque psoriasis	NA
Sotiriou et al[7]	14	AZ: 7 pts Pfizer: 6 pts Moderna: 1 pt	2nd dose: 12 pts 1st dose: 2 pts	3–32	13 pts with plaque psoriasis, 1 pt with guttae psoriasis	9 pts w/o treatment, 5 pts with topical treatment (steroid, calcipotriol/ betamethasone)	Exacerbation of pre-existing plaque psoriasis	5 pts treated with topical calcipotriol/ betamethasone, 9 pts treated with phototherapy
Perna et al[4]	1	Pfizer	1	5	Plaque psoriasis	Emollient	Acute generalized pustular psoriasis	Cyclosporin, Infliximab
Elamin et al[5]	1	AZ	1	21	None	None	Acute generalized pustular psoriasis	Acitretin
Ricardo et al[8]	1	Pfizer	2	7	None	None	De novo nail psoriasis	Clobetasol 0.05% ointment
Our patient	2	1st dose: Moderna 2nd dose: Pfizer	2	7	Plaque psoriasis	None	Erythrodermic psoriasis	Acitretin

Abbreviations: AZ, AstraZeneca; NA, not available; pt(s), patient(s); w/o, without.

role in the epidermal changes in psoriasis. We hypothesized that these mechanisms were also responsible for activating the immune system and provoking psoriasis in our case. We also speculated that the mixing of the BNT162b2 and mRNA-1273 vaccines induced a shift from the Th1 to the Th2 pathway, leading to erythrodermic psoriasis in our patient.

Although vaccination against the severe acute respiratory syndrome Coronavirus 2 is crucial to tackle the ongoing COVID-19 pandemic, we believe that it is important to caution patients with psoriasis (especially those who are not receiving any systemic treatment) against the rare, but possible exacerbation of their disease. Future studies must investigate the causal relationships between COVID-19 vaccines and GEP.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTION

Tong Ba Tran: acquisition of data, drafting the manuscript, and giving final approval of the version to be published. Nhi Thi Uyen Pham: acquisition of data, drafting the manuscript, and giving final approval of the version to be published. Huy Ngoc Phan: acquisition of data, drafting the manuscript, and giving final approval of the version to be published. Hao Trong Nguyen: drafting the manuscript, revising it critically for important intellectual content, and giving final approval of the version to be published.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

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

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