

## Generalized eczematous reactions to the Pfizer-BioNTech COVID-19 vaccine

Dear Editor,

Immediate and delayed local injection site reactions to mRNA vaccines against SARS-CoV-2 have been previously reported.<sup>1–3</sup> However, eczematous cutaneous reactions after COVID-19 mRNA vaccines have only been described once in the literature.<sup>4</sup> The previously described patient had moderate-to-severe atopic dermatitis on dupilumab and flared after vaccination. His atopic dermatitis flare resolved with oral glucocorticoids. Here, we present two patients who developed generalized eczematous eruptions after both doses of the (Pfizer-BioNTech, Brooklyn, NY, USA) COVID-19 vaccine.

This first patient was a 43-year-old man with a history of seasonal allergies who developed a pruritic eruption on his extremities 3 days after his first dose of the Pfizer-BioNTech COVID-19 vaccine. He presented to the dermatology clinic on day 5 post-vaccine due to progression of the eruption. He had a family history of atopic dermatitis but no personal history of atopic dermatitis. On examination, he had pink patches and papules with overlying excoriation on his back, arms and legs (Fig. 1). A skin biopsy showed spongiosis, acanthosis, parakeratosis and an inflammatory infiltrate consistent with eczematous dermatitis. He was treated with topical glucocorticoids and oral antihistamines and improved over several weeks. He received the second



**Figure 1** Generalized eczematous reaction on the back and shoulder.

vaccine dose 7 weeks after his first dose, and two weeks after the second dose, he had a recurrence of the eruption that again responded to topical glucocorticoids.

The second patient was a 51-year-old woman with a history of dyshidrotic eczema who presented with a pruritic eruption 4 days after her first Pfizer-BioNTech COVID-19 vaccine dose. She developed pruritus on her lower back hours after receiving the vaccine. The rash progressed over several days. On examination, pink papules coalescing into plaques were noted on the left lower back (Fig. 2). Skin biopsy revealed spongiosis with a mainly superficial perivascular lymphocytic infiltrate consistent with eczematous dermatitis. She was treated with topical glucocorticoids and improved. She received the second Pfizer-BioNTech COVID-19 vaccine dose 4 weeks after the first dose and had a recurrence of the rash 4 days later; the eruption was more generalized and involved the posterior neck, chest, flanks, back and lower extremities. She was treated with an oral prednisone taper and her symptoms resolved.

Despite experiencing generalized reactions, neither patient developed serious adverse events after the first or second vaccine dose. Both of these cases suggest that patients who develop generalized eczematous reactions to the Pfizer-BioNTech COVID-19 vaccine can safely receive the second dose. We did observe a recurrence in the eczematous dermatitis with the second vaccine dose, but these recurrences were responsive to topical and oral glucocorticoids. This contrasts with what has been observed with delayed large local reactions, in which most patients with a first-dose reaction did not develop a second-dose reaction.<sup>2</sup> Interestingly, both patients in this series had no involvement of the site of injection.

While the cause of these generalized eczematous reactions is unknown, the Pfizer-BioNTech vaccine may act as an environmental trigger in a genetically susceptible individual. In both



**Figure 2** Generalized eczematous reaction on the lower back.

cases, the patients had a personal or family history of atopy, perhaps making them more susceptible to an eczematous reaction. It is unknown if this reaction may also occur with the Moderna mRNA COVID-19 vaccine. As more of the population is vaccinated against COVID-19, rare reactions are likely to surface and it is important to study these reactions to facilitate optimal management of patients who develop them. In this series of two patients who developed generalized eczematous reactions to the Pfizer-BioNTech COVID-19 vaccine, the reaction occurred with both doses, was managed by oral or systemic glucocorticoids and did not prevent safe administration of both doses of the vaccine.

### Patient consent

The patients in this manuscript have given written informed consent to the publication of their case details.

### Conflict of interest

None to declare.

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## Erythema multiforme after CoronaVac vaccination

Dear Editor,

In January 2021, SARS-CoV-2 vaccine, CoronaVac, developed by Sinovac Life Sciences (Beijing, China) was approved for the use in Brazil by its National Health Surveillance. It is an inactivated SARS-CoV-2 virus adsorbed on aluminium hydroxide and diluted

in sodium chloride and phosphate-buffered saline.<sup>1</sup> Like other novel vaccines against COVID-19, it can induce cutaneous adverse reactions, generally mild.<sup>1</sup> Erythema multiforme (EM) is an acute and usually self-limited immune-mediated mucocutaneous disorder.<sup>2</sup> It is related to infections in 90% of cases – mainly herpes simplex virus (HSV) infections – and in 10% of cases, to drugs.<sup>2</sup> Unusually, it has also been documented following the vaccination.<sup>3</sup> We report a case of EM after CoronaVac vaccination.

A 75-year-old man with hypertension received both doses of the COVID-19 vaccine, CoronaVac: the first on February 12th and the second on March 6th. He was also in the use of ramipril 5 mg for the past 7 years. He had no adverse reactions after the first dose. However, five days after the second dose, he started with pruriginous, raised edematous lesions, with two colour zones and poorly defined borders, symmetrically in his knees (Fig. 1) that then spread to his face (Fig. 2) and trunk. He denied systemic symptoms, intake of new medications, and had no signs suggesting any infections. Mucous membranes were not affected. Also, he had neither medical history of herpes simplex infections, nor cutaneous adverse reactions to previous vaccines. A punch biopsy was performed and showed a lymphohistiocytic infiltrate surrounding the superficial dermal vessels. Laboratory tests, like erythrocyte sedimentation rate, white blood cell count, liver enzyme levels and serologies, were normal. A diagnosis of erythema multiforme minor was made, and treatment with topical corticosteroids and oral antihistamines for symptomatic relief was performed.

Almost, all vaccine components can be potential triggers to allergic reaction, but they are usually caused by the inert components (excipients).<sup>4</sup> Adjuvants, like aluminium salt present in CoronaVac, are responsible for type IV hypersensitivity.<sup>4</sup> Polyethylene glycol (macrogol), in the currently available Pfizer (New York, NY, USA)-BioNTech (Mainz, Germany) and Moderna, was suggested to cause immediate hypersensitivity reactions and also delayed-type reactions like pseudoallergic or non-IgE-mediated urticaria.<sup>4,5</sup>

Recently, EM was registered after mRNA-based COVID-19 vaccines: three cases after Moderna first dose<sup>6</sup> and a case of EM-like lesions in a patient with lupus erythematosus (Rowell's syndrome) after Pfizer first dose.<sup>7</sup> But until now, we have no data about EM after the CoronaVac vaccine. Although a fortuitous occurrence cannot be totally excluded in our case, the temporal association, absence of HSV infection history and other identifiable triggers make very likely the eruption, was caused by CoronaVac.

The aetiology of EM is unclear, but appears that in genetically predisposed individuals, and a trigger (usually infection) induces cell-mediated immune processes against antigens, via CD4 type 1 T-helper cells, release of IFN- $\gamma$  and then recruitment of autoreactive T cells.<sup>3</sup> IFN- $\gamma$  was also detected as an indicator of T-cell responses after CoronaVac vaccination.<sup>1</sup> Hence, we hypothesize