

Due to our knowledge, this is the first case of EGR related to COVID-19. The compelling clinical manifestation of EGR in our patient was directly related to the SARS-CoV-2 infection and totally disappeared just after the resolution of the case. No signs of any underlying malignancies were detected.

In our opinion, EGR should no longer be considered as an obligate paraneoplastic syndrome as the cases not associated with neoplasm are clearly not so uncommon.<sup>1</sup> In addition to searching an underlying neoplasm, clinicians should be aware of the possibility of other associations.<sup>1</sup> COVID-19 should be considered in patients with EGR as an underlying cause of the disease.

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

### Conflicts of interest

Rafaela Castro e Silva, Gabriela Castro e Silva, Maria Celeste de Castro Silva and Omar Lupi do not have any conflict of interests regarding this submission.

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## Cutaneous reactions following CoronaVac COVID-19 vaccination: a case series of six healthcare workers from a single centre

The significant impact of the COVID-19 pandemic on public health, the economy and society required rapid action and the development of vaccines in an unprecedented time frame. While traditional vaccine development may take 15 years or more, vaccine development for SARS-CoV-2 has been reduced to 12–18 months with an accelerated timeline.<sup>1</sup>

Phase 1/2 clinical trials of the inactivated vaccine candidate CoronaVac COVID-19 vaccine showed that this vaccine is safe and tolerable, and phase 3 clinical trials were conducted in Brazil, Turkey and Indonesia.<sup>2</sup> Announced emergency use authorization for CoronaVac on 13 January 2021 in Turkey.<sup>3</sup> Vaccination was initiated primarily in healthcare workers and higher risk groups. The vaccine was given in two doses (days 0 and 28).

Here, we present a case series of 6 patients who developed a cutaneous reaction after CoronaVac COVID-19 vaccination of healthcare workers from a single centre. The demographic data of the patients and the clinical course of the cutaneous reactions are detailed in Table 1.

One patient developed a maculopapular rash one week after the initial vaccination and resolved spontaneously within one week. One day after the second vaccination, the rashes recurred with atypical targetoid lesions, more extensive skin involvement and an erythematous patch on the upper palate. Histological examination revealed interface dermatitis (Figure 1a–c). There was initial concern about possible progression to Steven Johnson syndrome, and however, as there was no further mucosal involvement or skin necrosis, the final diagnosis was erythema multiforme major, and she had good clinical recovery with systemic corticosteroid.

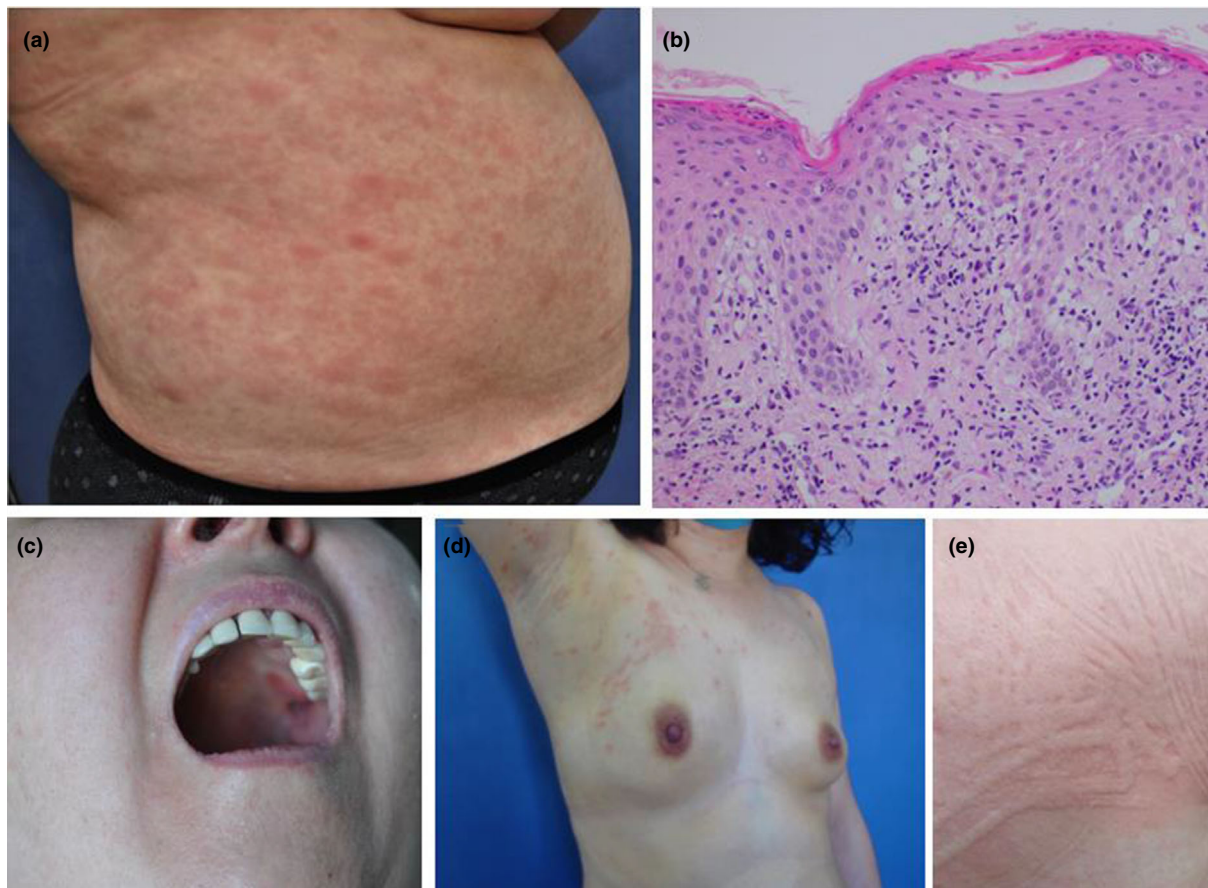
One patient developed erythematous scaly papules located along the skin cleavage lines with two plaques resembling the herald patch on the trunk 4 days after the first dose of vaccine (Figure 1d). The morphological appearance of the lesions and histopathological findings were consistent with classical pityriasis rosea. The rashes faded within three weeks, but reactivated 4 days after the second vaccination, and all lesions resolved completely within 8 weeks.

Three patients presented with symptoms of urticaria after the first vaccination and one patient after the second vaccination (Figure 1e). None of the 4 patients had a prior history of urticaria. Three of the patients were subsequently diagnosed with chronic urticaria as symptoms had persisted for more than 6 weeks.

**Table 1** The demographic data of the patients and the clinical course of the cutaneous reactions

Case age /sex	Cutaneous manifestation	Distribution	The clinical course of the lesions during the vaccination process	Medical history	PCR proven COVID-19 infection
45/F	Erythematous dusky macules and papules and targetoid lesions  Erythematous patch	Symmetric, trunk, upper and lower limbs  Upper palate	Onset 3 days after the first dose, improved but recurred 1 day after the second dose with increased severity	Skin rashes with NSAID	No
45/F	Two oval thin plaques with a peripheral collarette scaling reminiscent of a herald patch  Multiple scaly erythematous plaques	Right breast and scapula  Symmetric, along skin cleavage lines on trunk and upper limbs	Onset 4 days after the first dose, gradually partially resolved but reactivated again 4 days after the second dose.	Unremarkable	Yes
29/F	Linear weals	Along the shape of the scratching and rubbing areas	Onset 4 h after the first dose. She refused second dose.	Penicillin and metal allergy, polymorphic light eruption	No
32/F	Weals  Angioedema	Trunk, upper and lower limbs  Both eyes(periorbital)	Onset 12 weeks after the first dose. Persisted with worsening after the second dose.	Hashimoto thyroiditis	Yes
48/F	Weals  Angioedema	Trunk, upper and lower limbs  Both eyes(periorbital) and lips	Onset 4 h after the first dose. Persisted with worsening after the second dose.	Asthma, allergic rhinoconjunctivitis, latex and metal allergy, Hashimoto thyroiditis	No
26/F	Weals	Ears and upper limbs	Onset 2 h after the second dose, improved within a week.	Unremarkable	No
Histopathology	Diagnosis		Treatment	Follow-up period/current situation	
Parakeratosis, spongiosis, lymphocytic exocytosis, parabasal layer vacuolar changes, apoptotic keratinocytes in the dermis and moderate mononuclear inflammation in the dermis	Erythema multiforme major		Oral antihistamine, systemic and topical corticosteroid	8 weeks/ resolution	
Focal parakeratosis with exocytosis of lymphocytes, spongiosis in the epidermis, and extravasated red blood cells in the dermis	Pityriasis rosea		Topical corticosteroid	8 weeks/ resolution	
None	Symptomatic dermographism		Oral antihistamine	12 weeks/ improvement	
None	Chronic spontaneous urticaria		Oral antihistamine and systemic corticosteroid	9 weeks/ resolution	
None	Chronic spontaneous urticaria		Oral antihistamine and omalizumab 300 mg/4 weeks	12 weeks/ improvement	
None	Acute urticaria		None	1 week/ resolution	

F, Female.



**Figure 1** (a-c) In a patient with erythema multiforme major, clinical presentation of dusky red macules and papules, targetoid lesions on the trunk and erythematous plaque on the upper palate, and histopathological appearance of parakeratosis, spongiosis, lymphocytic exocytosis, parabasal layer vacuolar changes, moderate mononuclear inflammation in the dermis (HE,  $\times 200$ ). (d) In a patient with pityriasis rosea, multiple erythematous scaly papules located along the skin cleavage lines with herald patch on the right breast. (e) In a patient with symptomatic dermographism, weals along the shape of the scratching and rubbing areas

In comprehensive history evaluations, there was no other condition (e.g. infection or use of other medication) explaining the cause of skin rash in any patient.

Vaccines are the most important intervention against preventable infections in the protection of public health, but vaccine-related adverse events are a common problem in clinical practice. Fortunately, serious acute or delayed onset systemic reactions are extremely rare. The most common reactions after immunization are local reactions and non-immediate skin reactions such as delayed urticaria or maculopapular eruptions. Delayed reactions are generally considered to be self-limiting conditions that do not contraindicate the administration of booster doses of the same vaccine.<sup>4,5</sup> Delayed cutaneous reactions were evident in these 6 patients who developed cutaneous adverse events among the 4257 vaccinated healthcare workers. Except for one patient with acute urticaria, other patients applied to our

outpatient clinic because they suffered from severe or prolonged skin rash and itching. However, the actual incidence of cutaneous reactions is possibly higher as patients with mild self-limiting symptoms may not have applied or sought medical care.

CoronaVac vaccine-related cutaneous adverse events have been reported very few, and cutaneous reactions following inactivated CoronaVac vaccine have been well documented in this series. As vaccination studies continue, cutaneous reactions are also likely to continue to occur. Therefore, it is very important for dermatologists to recognize and manage skin rashes associated with the CoronaVac COVID-19 vaccine and inform patients.

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## A Bullous Eruption following the Pfizer-BioNTech COVID-19 vaccination

Dear Editor,

On 2 December 2020, the Medicines and Healthcare products Regulatory Agency (MHRA) authorized the use of a modRNA – nucleoside modified messenger RNA (mRNA) COVID-19 vaccine; Pfizer-BioNTech. Prior to this, no mRNA vaccines had been authorized for use in humans.<sup>1</sup>

As of June 2021, 66 million COVID-19 vaccinations have been administered within the UK.<sup>2</sup> Currently, approved vaccines for use in the UK include Pfizer-BioNTech, Oxford/AstraZeneca and Moderna variants. An ongoing multinational randomized controlled trial assessing the safety of the Pfizer-BioNTech vaccine reported few localized cutaneous reactions at the injection site, but no significant adverse cutaneous reactions. The data from this study suggested a two-dose regimen of the Pfizer-BioNTech vaccine was safe and effective in 95% of cases.<sup>3</sup>

We report a case of an acute widespread bullous eruption following administration of the second Pfizer-BioNTech vaccine in a 52-year-old Caucasian female. The patient developed a local site reaction 3 hours postvaccination, and within a few days, a



**Figure 1** Widespread erythematous maculopapular eruption originating on the right arm (vaccination site) with areas of exfoliation.

widespread florid maculopapular, erythematous eruption with face and mucous membrane sparing (Fig. 1). Past medical history included Type 2 Diabetes Mellitus and morbid obesity (BMI 58.8 kg/m<sup>2</sup>). The patient reported a similar, but localized, self-limiting cutaneous reaction following an influenza vaccination some years previously.

Laboratory investigations revealed a mild transaminitis with alanine aminotransferase of 54 IU/L and an eosinophilia  $1.0 \times 10^9/L$ . A skin biopsy was taken from the left shoulder showing a dual pattern of inflammation with spongiotic and interface dermatitis. The patient was initiated on topical clobetasol 0.05% ointment and 50:50 white soft paraffin: liquid paraffin.

The patient was re-reviewed 1 week later, unwell with fatigue and a marked deterioration of the rash, with further extension and widespread bullae initiating on the upper legs (Fig. 2). The patient was admitted and commenced on oral prednisolone (50 mg). Within three days of admission, there was resolution of the transaminitis and eosinophilia, with marked improvement