


had a slightly higher incidence of facial skin problems than those with oily skin. Changes in the facial microbiome might partly explain the skin problems caused by long-term mask wearing.

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### Conflict of interest

All authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Three cases of vesiculobullous non-IgE-mediated cutaneous reactions to tozinameran (Pfizer-BioNTech COVID-19 vaccine)

Dear Editor,

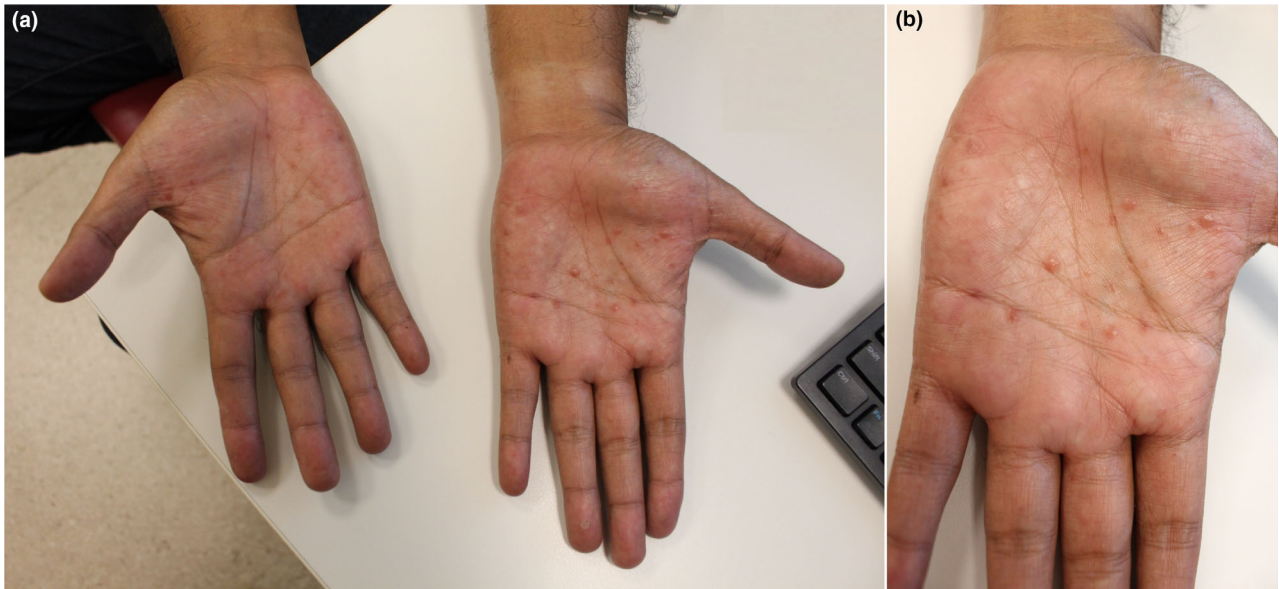
There is a global uptake of vaccination against coronavirus disease 2019 (COVID-19). The Phase III trial of tozinameran, a ribonucleic acid (RNA) vaccine, demonstrated a risk of anaphylaxis at 11.1 cases per million doses.<sup>1</sup> Little is known regarding various non-IgE-mediated cutaneous reactions arising from the use of these vaccines. We report three cases of non-IgE-mediated cutaneous reactions following tozinameran administration, in a tertiary hospital in Singapore.

A 51-year-old gentleman developed deep-seated vesicles over his palms 1 day after administration of the second dose of tozinameran. Examination revealed scattered deep vesicles over bilateral palms, with focal desquamation (Fig. 1a,b). He was diagnosed with acute dyshidrotic eczema and treated with topical betamethasone dipropionate ointment.

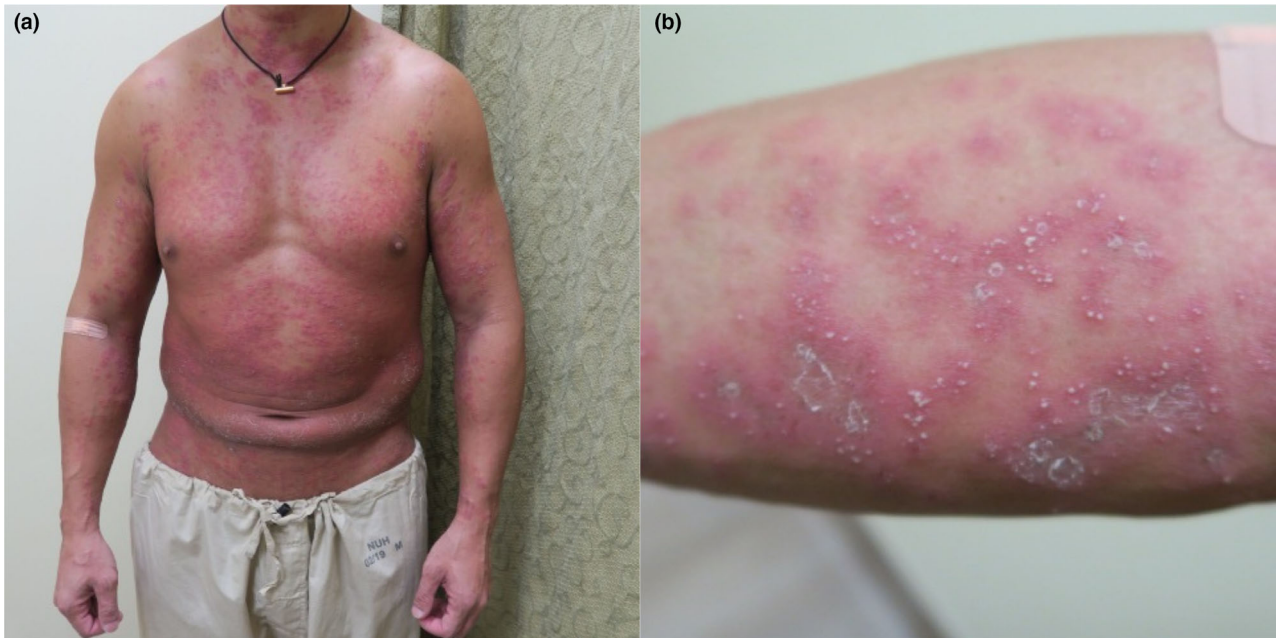
A 70-year-old woman was admitted to the hospital for an acute flare of bullous pemphigoid 2 weeks following administration of the first dose of tozinameran. She had a known history of biopsy-proven bullous pemphigoid, which was controlled on tapering, low-dose prednisolone. Other drug and infective histories were unremarkable. Inpatient admission was required. Treatment consisted of prednisolone dose escalation to 0.5 mg/kg/day and application of clobetasol 0.05% cream.

A 38-year-old man presented for fever and pruritic rashes, 5 days after administration of the second dose of tozinameran. Localizing infective symptoms were absent. Drug history was otherwise unremarkable. Erythematous scaly plaques studded with non-follicular pustules and desquamative scales over his trunk and limbs (Fig. 2a,b) was associated with marked neutrophilia. Fungal scrape was negative. Histology was supportive of the diagnosis of acute generalized exanthematous pustulosis (AGEP). Clinical resolution was achieved with topical mometasone cream.

These cases of non-allergic cutaneous reactions consisting of vesiculobullous eruptions demonstrate varying degrees of severity. A case series of 12 patients with delayed large local reactions to mRNA-1273 vaccine described an isolated patient developing papules over the palms 4 days after receiving the vaccine.<sup>2</sup> Eczema flares following vaccination for mumps, measles and rubella have been reported.<sup>3</sup> The pathomechanism of MMR-vaccine aggravating eczema was postulated to be that of increased interleukin-4 levels following infection by the live attenuated virions. Vaccinations may instigate a vigorous host immune response, thereby dysregulating the delicate Th1 and Th2



**Figure 1** (a) Erythematous vesicles on bilateral palms. (b) Deep-seated tense vesicles on the palmar aspect.



**Figure 2** (a) Extensive erythematous plaques with crops of non-follicular pustules over the trunk and limbs of this patient with AGEF. (b) Non-follicular pustules on an erythematous plaque.

lymphocytic balance in these atopic individuals. The mechanism for RNA vaccine inducing vesicular eczema remains unknown.

Drug-induced bullous pemphigoid remains incompletely understood.<sup>4</sup> The pathomechanistic concept of molecular mimicry

with the RNA vaccine is postulated, with SARS-CoV-2 spike proteins produced leading to activation of CD4+ T cells and initiation or rekindling of the autoimmune cascade. Bullous pemphigoid following vaccinations usually has a short latency of days.<sup>5</sup>

More than 90% of cases of AGEPE are drug-induced.<sup>6</sup> A case series of childhood AGEPE reported 2 cases of vaccine-related AGEPE,<sup>7</sup> while a pregnant woman of 10-week gestation developed AGEPE 1 day after influenza vaccination.<sup>8</sup> Tozinameran consists of lipid and mRNA nanoparticles. AGEPE may be induced via the RNA molecule, lipid vehicle or the eventual proteins arising from the translation of RNA. The propensity for components of the RNA vaccine to induce non-allergic cutaneous reactions remains insufficiently characterized. Preliminary case series have documented delayed large local reactions, termed 'COVID arm',<sup>2</sup> and various other reactions in a registry-based report of 414 cases.<sup>9</sup> These delayed cutaneous manifestations may be related to the host immune response instead of true vaccine allergies.

We opine that most delayed, mild non-IgE-mediated cutaneous reactions do not contraindicate further doses of the same vaccine, as these reactions are often transient and self-limiting, where the benefits of a completed vaccination schedule outweigh the potential morbidity following such reactions. Knowledge of both allergic and non-allergic cutaneous reactions to various COVID-19 vaccines is useful in the current mass vaccination exercises worldwide.

### Consent for publication

This manuscript has not been published and is not under consideration for publication elsewhere.

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

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## Psoriasis exacerbation after COVID-19 vaccination: a report of 14 cases from a single centre

Editor,

High COVID-19 vaccination rates are a prerequisite for the establishment of herd immunity.<sup>1</sup> Psoriasis patients seem to be more inclined to undergo COVID-19 vaccination, compared with matched controls suffering from other skin diseases and receiving immunosuppressive treatment (odds ratio, 1.32; 95% confidence interval: 1.28–1.36).<sup>1</sup> Twenty-one per cent of 713 asked psoriasis patients declared fear of potential postvaccination flare of their skin disease to be holding them back from receiving a COVID-19 vaccine.<sup>1</sup> Actual knowledge of the probability of this negative outcome occurring has largely been inadequate. As a number of vaccinated psoriasis patients steadily increase, the first data regarding this issue have been seeing the light of day.

Three European Medicines Agency-approved SARS-CoV-2 vaccines (Pfizer mRNA-BNT162b2; Moderna mRNA-1273; and AstraZeneca-Oxford AZD1222) have been administered to the Greek population from 27 December 2020 to 10 May 2021 (study lock date). Healthcare providers, followed by older individuals and those who were at the risk of severe COVID-19 infection due to comorbidities (including psoriasis under immunosuppressive treatment), were the first to be vaccinated in Greece.

Fourteen patients (mean age, 66.93; standard deviation, 9.68; females, 64.29%) (Table 1) presented to the emergency department of our hospital from 1 January to 10 May 2021 with sudden onset of a generalized papulosquamous rash, which was clinically diagnosed as psoriasis (Fig. 1). Of these, nine patients had had known mild psoriasis (mean duration, 16.39 years; standard deviation, 5.23), which had been left without treatment for over a year. Five patients had only been receiving topical treatment (steroids, calcipotriol/betamethasone), with which