Pfizer/BioNTech-associated perniosis in two young adults with re-challenge evidence

Dear Editor,

The employment of novel mRNA delivery with Pfizer/BioNTech (BNT162b2) and Moderna (mRNA-1273) SARS-CoV-2 vaccines has cultivated close scrutiny for adverse events. The novel immunogenic nature of the SARS-CoV-2 virus and its peculiar cutaneous clinical sequelae has further compounded this behaviour. Authors of the American Academy of Dermatology (AAD) and the International League of Dermatological Societies (ILDS) recently published a registry demonstrating a breadth of cutaneous reactions related to the mRNA vaccines.[1] Unsurprisingly, the most frequent is local injection site reactions, seen also in Bogdanov *et al.*,[2] but the degree of atypical adverse events, such as erythromelalgia in 6%,[1] is striking. Chilblains, or perniosis, are an infrequent reaction in this registry of 414 patients; it was seen eight times as frequently in Pfizer/BioNTech vaccination (8.8%) than amongst patients who received Moderna (1.1%). In contrast, in the setting of natural infection from a registry of 716 patients from 31 countries, up to 18% and 33% of patients with either a confirmed or suspected natural infection, respectively, developed a pernio-like reaction; in the setting of natural infection in this registry, and it was the second most common COVID-19-associated dermatologic manifestation.[3]

We report two cases of Pfizer/BioNTech vaccine-associated chilblains in previously healthy patients, both with re-challenge evidence and negative viral nasopharyngeal detection. The 31- and 33-year-old men developed lower extremity dorsal acral and periungual pruritus as well as slight tenderness with erythema and oedema at days 5 and 7 following their first vaccine dose. In both cases, the erythema, pruritus and slight tenderness subsided almost entirely by the second dose (28 days later). However, 24-h following their second dose, both had a recurrence of symptoms; in one case, this proceeded to the point of ulceration (Fig. 1). Natural resolution was achieved within 6 weeks in both patients with no residual skin or neurovascular changes. The Naranjo Algorithm was used to score the probability of an adverse drug reaction, which yielded a score of 6 (probable) in both cases.[4]

The morphological findings in vaccine-induced chilblains appear indistinguishable from idiopathic perniosis and that associated with autoimmune connective tissue disease (AiCTD) with accompanying histologic lymphocytic vasculitis.[5]

Both the Pfizer/BioNTech and Moderna (mRNA-1273) vaccines encode spike protein antigens with a very high degree of similarity between the generated antibody responses targeted at epitopes from the receptor-binding domain.[6] While both cases reported here were secondary to the Pfizer/BioNTech vaccine, as well as those reported by McMahon *et al.*[1] ($n = 2$) and Lesort *et al.*[7] ($n = 1$), we suspect that this cutaneous adverse event is not limited to Pfizer/BionTech, but instead represents a phenomenon of immunogenic response; further work is needed to better understand the pathogenesis and relevance to systemic immunity.

In conclusion, we report two cases of SARS-CoV-2 perniosis associated with mRNA Pfizer/BioNTech vaccine, which recurred with re-challenge and were self-limited. Vaccine-related perniosis appears to be an indolent cutaneous reaction, which abates in short term, but further documentation and awareness are needed to understand the natural history in larger case numbers.

Acknowledgement

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

Conflict of interest

None.

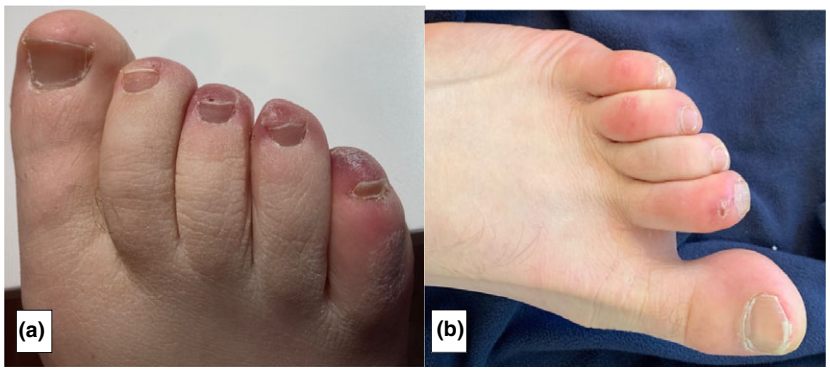

Figure 1 Pernio-like lesions on the toes of two male patients, 24 h post-Pfizer/BioNTech vaccine. Both cases demonstrate digital oedema and deeply erythematous-violaceous plaques on the dorsal, periungual and distal toes (Patient a; initial presentation), as well as ulceration of the second and later multiple digit (Patient b; 96 h postrechallenge).

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Not applicable, and no new data were generated.

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Herpes zoster viral infection after AZD1222 and BNT162b2 coronavirus disease 2019 mRNA vaccines: a case series

Dear Editor,

We report the first cases of Varicella-zoster viral (VZV) infection after AZD1222 and BNT162b2 coronavirus disease 2019 (COVID-19) mRNA vaccines in Greece. As the World Health Organization declared the COVID-19 as a pandemic, the production of a safe and effective vaccine COVID-19 became a global priority.[1] In December 2020, the European Medicines Agency first approved the BNT162b2 (Pfizer-BioNTech COVID-19 mRNA) vaccine and the AZD1222 (Oxford/AstraZeneca (University of Oxford, Oxford, UK) COVID-19) vaccine.[2] There is a great variety of cutaneous reactions after COVID-19 vaccination,[1,2] with only a few cases of Varicella-zoster viral infection (VZV) reported.[3-9] Given the importance of widespread vaccination, recognition and understanding of these novel vaccines' adverse events are crucial. In this brief report, we present a case series of VZV infection after AZD1222 and BNT162b2 COVID-19 mRNA COVID-19 vaccination in Heraklion, Crete, Greece.

A retrospective case-series study was performed at the Dermatology Department at the University Hospital of Heraklion in

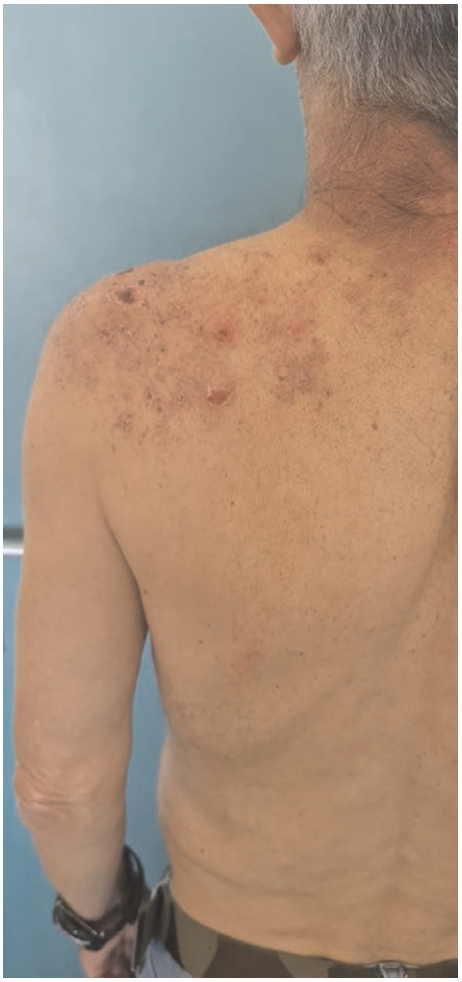

Figure 1 Vesicles, erosions and erythematous plaques in clusters on the left side of the upper back and arm on a male patient after AZD1222 vaccination, evocative of a herpes zoster viral (VZV) infection.