Table 1 Two patients developing anaphylactoid reactions after mRNA-1273 vaccination and receiving omalizumab prior to second dose

	Patient #1	Patient #2
Age in years	27	31
Sex	Female	Female
History of hypersensitivity	None	Type IV (nickel)
Time to systemic reaction after 1st dose	1 h	10 days
Symptoms	AE of lips and tongue incl. dyspnoea, flush	Urticarial rash with subsequent AE of tongue and upper lids
Treatment	i.v. CS and AH	Topical and oral CS, oral AH
Serology: total IgE, specific IgE to aeroallergens, tryptase levels (Immuno-CAP FEIA, Thermo Fisher Scientific Inc., Waltham, MA, USA)	NAD	NAD
Skin prick test (after suff. washout period)	Negative for mRNA-1273	Negative for mRNA-1273
BAT (mRNA-1273, PEG 2000, DMG PEG 2000; Bühlmann Laboratories AG, Schönenbuch, Switzerland)	Negative	Negative
Pretreatment with omalizumab in days to 2nd dose	2	7
Symptoms after 2nd dose	None	Solely localized urticaria after 8 days
SARS-CoV-2 nucleocapsid-specific IgG after 2nd dose	Negative	Negative
SARS-CoV-2 spike-specific IgG after 2nd dose	>384.00 BAU/mL	>384.00 BAU/mL
Neutralization titre after 2nd dose	80	320

Two patients who developed AE/AE with urticaria after first dose of mRNA-1273 and subsequently received pretreatment with omalizumab to prevent a possible anaphylactoid reaction listed with relevant clinical parameters. Antibody titre tests were performed to evaluate efficacy of mRNA-1273 vaccination: Patient sera were tested for SARS-CoV-2 nucleocapsid-specific IgG using SARS-CoV-2 IgG chemiluminescent microparticle immunoassay from Abbott performed on an ARCHITECT i2000 SR. Euroimmun Anti-SARS-CoV-2-QuantiVac-ELISA was used to measure IgG levels against SARS-CoV-2 spike S1 after the second vaccination. Neutralizing antibody titres were tested using an in-house serial dilution endpoint neutralization test performed under BSL-3 safety conditions.

AE, angioedema; AH, antihistamines; BAT, basophil activation test; CS, corticosteroids; DMG, dimyristoyl glycerol; i.v, intravenous; IgE, immunoglobulin E; NAD, no abnormality detected; PEG, polyethylene glycol.

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Small vessel vasculitis related to varicella-zoster virus after Pfizer-BioNTech COVID-19 vaccine

Dear Editor,

We read with great interest the article by Ackerman *et al.*[1] regarding the occurrence of persistent maculopapular rash few hours after receiving the vaccine.[1]

We herein report a case of atypical varicella-zoster virus skin infection inducing a small vessel vasculitis after first dose of Pfizer-BioNTech COVID-19 vaccine. An 84-year-old female patient, with medical history of chronic kidney disease and depressive disorder, received the first dose of Pfizer-BioNTech (Mainz, Germany) COVID-19 vaccine. Few hours later, she developed burning pain on the distal part of right leg and foot, followed by multiple non-confluent purpuric papules and vesicles in the same sites (Figs 1 and 2). Clinical examination did not show signs of systemic involvement and serum tests showed varicella-zoster virus (VZV) IgM and IgG antibodies positivity and high levels of liver enzymes (2N). Punch biopsy of right lower leg was performed and histopathologic examination showed intraepidermal spongiosis with acantholytic keratinocytes,

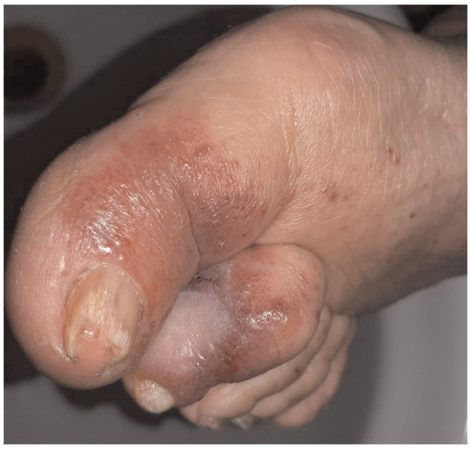

Figure 1 Small cell vasculitis varicella-zoster virus – related on right foot.

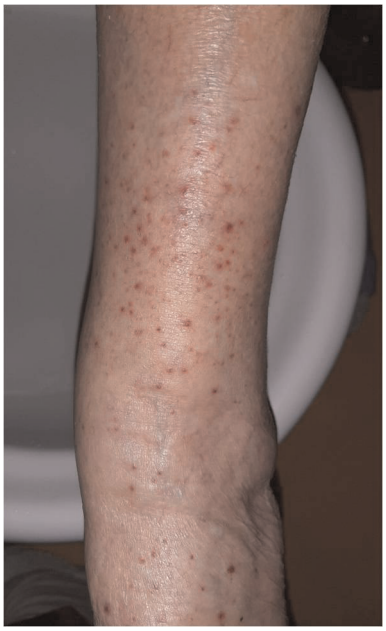

Figure 2 Small cell vasculitis varicella-zoster virus – related on right leg.

multinucleation and intranuclear inclusion bodies. Superficial dermis showed vasculitic damage with inflammatory infiltrate, fibrin exudation, extravasated erythrocytes and leucocytoclasia. Direct immunofluorescence test was negative. Polymerase chain reaction of a skin swab for VZV resulted positive. Therefore, the diagnosis of atypical herpes zoster associated with cutaneous vasculitis was made. Treatment was started with famciclovir 500 mg orally every 8 h for 10 days. A clinical improvement of her skin lesions was achieved in few days, and they were completely resolved 2 weeks later despite the persistence of local pain. Because of the persistence of local pain and liver involvement, the patient refused to take the second dose of vaccine.

Although Pfizer-BioNTech COVID-19 vaccine is considered safe, side-effects, especially dermatological ones, are currently poorly characterized. Clinical trials have reported that the most frequent cutaneous side-effects are injection-site reaction and pruritus; cases of allergic reactions such as urticaria and diffuse erythematous rash have been described.[2,3] Anecdotal cases of erythema multiforme and morbilliform rash have been reported in the literature.[1,4] In this article, we describe an atypical manifestation of herpes zoster infection after COVID-19 vaccine which caused small vessel vasculitis. Other cases of vasculopathies during VZV infection have been described,[5] and it is due to virus ability to infect endothelial cells directly, but no cases of herpes zoster vasculitis after COVID-19 vaccine have been reported. The age of patient and the immune reaction to vaccine would have induced a condition of immunosuppression, underlying virus reactivation. VZV infection must be considered in cases of purpuric lesions with acral localization and unilateral distribution, especially in immunocompromised patients and when other causes of vasculitis have been excluded. Early and correct diagnosis is important to reassure the patient and start timely therapy reducing the risk of postherpetic neuralgia.

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

Conflict of interest

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New-onset acral lesions on hands after administration of mRNA-1273 vaccine against SARS-CoV-2: clinical images and histopathological study of three cases

Dear Editor,

First approved vaccines against SARS-CoV-2 (*mRNA-1273 and BNT162b2*) consists of Messenger Ribonucleic Acid (mRNA), encoding the SARS-CoV-2 spike protein that penetrate cells and produce spike protein.[1] In these vaccines' clinical trials, chilblain-like lesions were not reported[2,3]; however, the World Health Organization warned of the possible of appearance of chilblain-like lesions during SARS-CoV-2 vaccination campaign.[4]

On February 2021, in Salamanca (Spain), hospital workers with ages ranging between 22 and 65 years were vaccinated. All of them were advised to notify any adverse effect associated to vaccination, including cutaneous manifestations. About 150 cutaneous manifestations were notified. Three patients with new-onset of acral inflammatory lesions on hands after SARS-CoV-2 mRNA-1273 vaccine were studied. Each patient underwent complete medical history and tests to discard other aetiologies. We performed SARS-CoV-2 tests included SARS-CoV-2 anti-spike antibodies with chemiluminescence immunoassay test (CLIA), and skin biopsies to each patient. Close follow-up was set up. Second dose of SARS-CoV-2 vaccine was not contraindicated.

Two of the three patients are female and all three have ages ranging between 29 and 54 years. The three patients are hospital

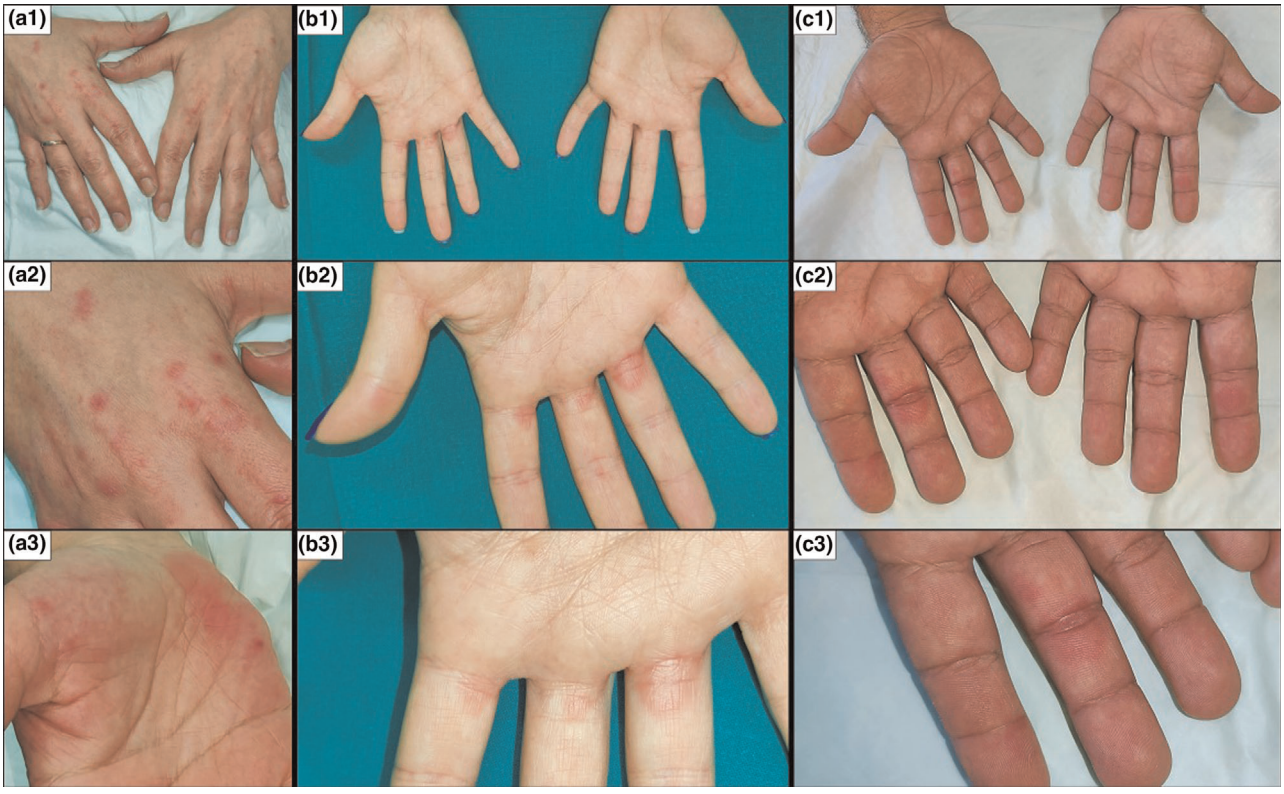

Figure 1 Clinical images of acral inflammatory lesions on the hands of the three patients. Patient 1 has itchy oedematous erythematous papules on the back of the hands and fingers (*a1*), mostly in the opposite hand to the vaccination arm (*a2*) and erythematous spots in palms (*a3*). The erythematous papules of this patient (*a1, a2*) could also be reminiscent of erythema multiforme-like lesions as well as chilblain-like lesions related to COVID-19. Patient 2 has a few similar lesions to the previous patient in the back of the hands. Patients 2 and 3 have itchy oedematous erythematous lesions in fingers (*b1, b2, b3, c1, c2, c3*). Most lesions in patients 2 and 3 appear on the opposite hand to the vaccination arm (*b2, b3, c2, c3*).

