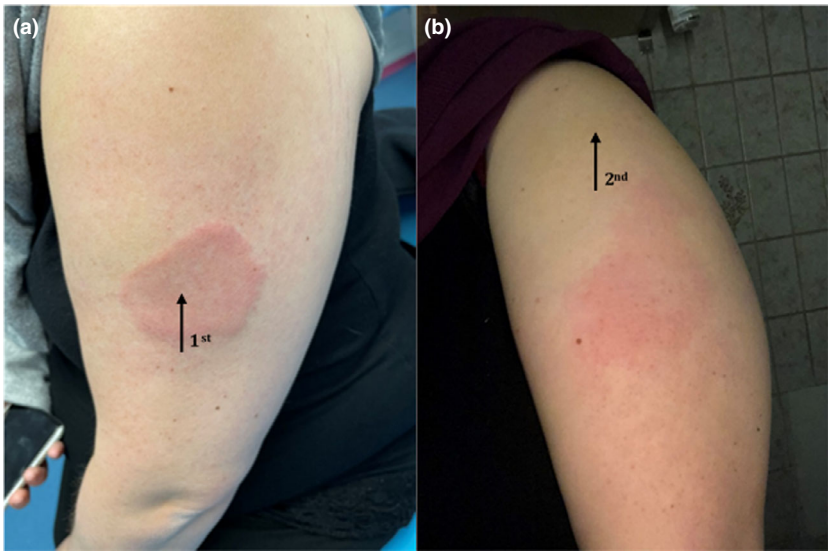

Fig. 1 Local skin reactions, left upper arm (patient photographs). (a) Day 12 after first COVID-19 vaccination; day 5 after SARS-CoV-2 infection. (b) Day 48 after first BNT162b2 vaccination; few hours after COVID-19 re-vaccination; Arrows indicate the two injection sites.

and vaccination needles should be chosen individually to ensure intramuscular bioavailability.

Funding source

The analyses were supported by grants from the Carlsberg Foundation (CF20-0045) and the Novo Nordisk Foundation (NFF205A0063505).

Acknowledgement

The patient in this manuscript has given written informed consent to publication of her case details. We thank Dr. Lene Heise Garvey for intellectual input.

Conflict of interest

None.

M. Gyldenløve,[1,*] L. Skov,[1] C.B. Hansen,[2] P. Garred[2]
[1]Department of Dermatology and Allergy, Herlev and Gentofte Hospital, University of Copenhagen, Hellerup, Denmark, [2]Laboratory of Molecular Medicine, Department of Clinical Immunology, Section 7631, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark
*Correspondence: M. Gyldenløve. E-mail: mette.gyldenloeve@regionh.dk

References

1 Blumenthal KG, Freeman EE, Saff RR, Robinson LB, Wolfson AR, Foreman RK. Delayed large local reactions to mRNA-1273 vaccine against SARS-CoV-2. *N Engl J Med* 2021; **384**: 1273–1277.
2 Hansen CB, Jarlhelt I, Pérez-Alós L *et al.* SARS-CoV-2 antibody responses are correlated to disease severity in COVID-19 convalescent individuals. *J Immunol* 2021; **206**: 109–117.
3 Zuckerman JN. The importance of injecting vaccines into muscle. *Br Med J* 2000; **321**: 1237–1238.
4 Pellini R, Venuti A, Pimpinelli F *et al.* Obesity may hamper SARS-CoV-2 vaccine immunogenicity; 2021. URL: https://www.medrxiv.org/content/10.1101/2021.02.24.21251664v1 (last accessed: 9 March 2021). preprint.
5 Poland GA, Borrud A, Jacobson RM *et al.* Determination of deltoid fat pad thickness. Implications for needle length in adult immunization. *JAMA* 1997; **277**: 1709–1711.

DOI: 10.1111/jdv.17341

Pityriasis rosea-like eruptions following vaccination with BNT162b2 mRNA COVID-19 Vaccine

Dear Editor,

COVID-19 has caused cutaneous symptoms in approximately 20% of patients, ranging from inflammatory and exanthematous eruptions to vasculopathic and vasculitic lesions.[1] Newly developed vaccines display high efficacy and low rates of adverse events. In the BNT162b2 (Pfizer, New York, NY, USA/BioNTech, Mainz, Germany) mRNA vaccine Phase III study, no participants reported cutaneous adverse events aside from injection site reactions.[2] We report two cases of cutaneous eruptions following BNT162b2 vaccination for COVID-19.

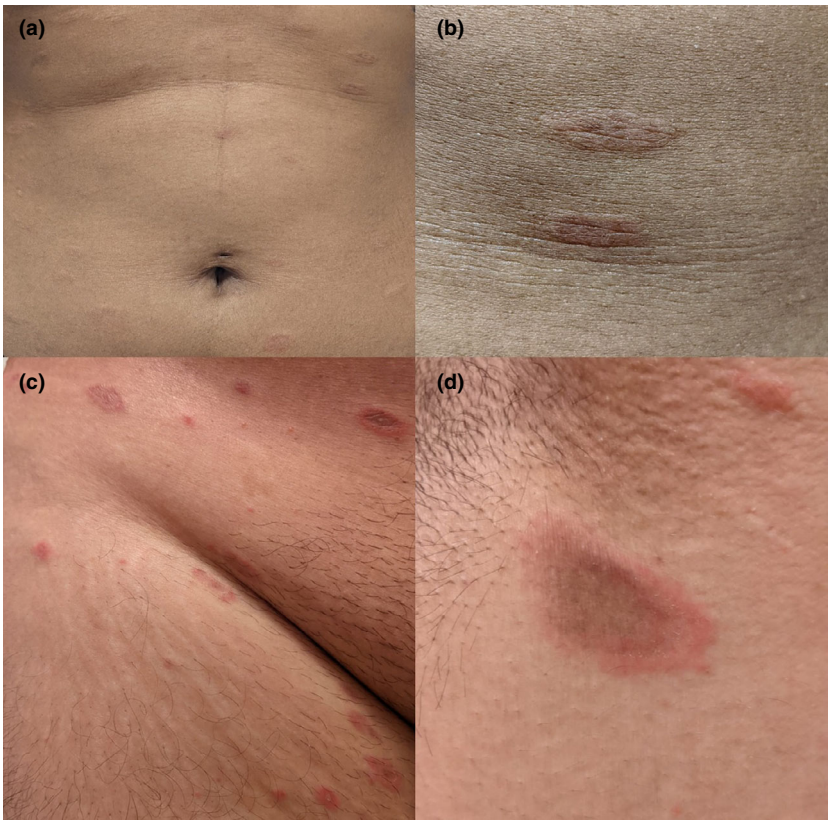

Figure 1 Clinical findings of pityriasis rosea-like eruption in the patients. (a) Patient 1: Thin red to tan oval plaques with peripheral scale on the trunk. (b) Patient 1: Close-up of a plaque. (c) Patient 2: Thin red to tan oval plaques with peripheral scale on the trunk and proximal thigh. (d) Patient 2: Close-up of plaques, with the hyperpigmented centre and trailing scale.

Our first case is a woman in her 20s with a history of alopecia areata who developed a large, pruritic, red and scaly plaque on her left arm at the inoculation site 2 days after her first dose of the vaccine. Subsequently, she developed small, red and scaly lesions on her trunk. Following her second vaccine dose, she experienced worsening of her symptoms, with increased pruritus and a growing number of lesions. On examination, she had multiple oval pink-to-tan-coloured thin plaques with peripheral scale on the trunk and proximal extremities (Fig. 1). The remainder of her physical examination was normal, including no oral mucous membranes lesions. She reported no preceding illness, no systemic symptoms, no sick contacts or no new drug exposures. Lesional biopsy demonstrated interface changes, with parakeratosis and scattered dyskeratotic keratinocytes (Fig. 2). She was diagnosed with a pityriasis rosea (PR)-like eruption and was started on topical corticosteroid therapy. After 2 weeks of therapy, she reported resolution of her pruritus and improvement of her lesions.

Our second patient, a previously healthy man in his 40s, noted an asymptomatic, red and scaly plaque on his lateral left axilla 3 weeks after administration of his second vaccine dose in his left shoulder. Two days later, he developed a widespread eruption of pruritic, small and scaly plaques. He experienced no preceding illness, no constitutional symptoms and had no known sick contacts or drug exposures. Examination demonstrated a classic herald patch on his left lateral axilla, as well as many symmetrically distributed smaller plaques with peripheral scale on the trunk and proximal extremities (Fig. 1). He had no oropharyngeal lesions. He was diagnosed with a PR-like eruption and prescribed doxycycline and bilastine. After 3 weeks of therapy, the patient had no new lesions and experienced resolution of pruritus.

Pityriasis rosea and PR-like eruptions are self-limited exanthematous papulosquamous rashes following Langer's lines and are most common in young adults. PR is associated with reactivation of either human herpesvirus (HHV)-6 or HHV-7, while PR-like eruptions are reactions to vaccinations or medications.[3,4] PR can be distinguished from PR-like eruptions by the presence of a herald patch and prodromal symptoms as well as the absence of pruritus.[3] Further investigations may be helpful

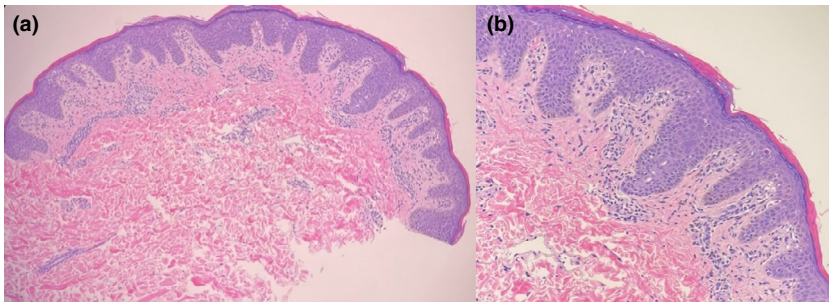

Figure 2 Histopathological findings of pityriasis rosea-like eruption in patient 1. Parakeratosis with minimal acanthosis and spongiosis of the epidermis. Few scattered dyskeratotic keratinocytes are seen in the lower epidermis. The papillary dermis shows melanin incontinence, perivascular lymphocytic infiltrate and rare scattered extravasated red blood cells. (a) haematoxylin-eosin, original magnification ×10. (b) haematoxylin-eosin, original magnification ×20.

as PR-like eruptions may have peripheral eosinophilia, interface dermatitis and eosinophils on histopathology, with no evidence of HHV-6 and HHV-7 systemic reactivation.[3] Our cases had overlapping features of both PR and PR-like eruptions.

COVID-19 has been associated with cases of PR and PR-like eruptions following the acute infection.[6,7] Skin biopsies may demonstrate positivity for the SARS-CoV-2 virus spike protein on endothelial cells and lymphocytes suggesting a direct relationship between SARS-CoV-2 infection and PR.[7] SARS-CoV-2 may also trigger PR by reactivation of HHV-6 or HHV-7.[5] PR eruptions have developed following vaccination for influenza and H1N1[8–10] and may be secondary to reactivation of HHV-6 and HHV-7, which may be detected in skin biopsies via in situ hybridization and immunohistochemistry.[9] Another possible cause for PR in the setting of vaccination is a T-cell-mediated response triggered by molecular mimicry from a viral epitope.[8]

Given worldwide vaccination efforts against COVID-19 with mRNA vaccines, it is important for doctors and patients to recognize possible adverse events including PR. Further study is required to confirm the causative link, including direct examination of tissue and serological studies for evidence of HHV-6 and HHV-7 reactivation.

Patient consent

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

Conflict of interest

The authors have no conflicts of interest to declare.

B.M. Cyrenne,* F. Al-Mohammedi, J.G. DeKoven, R. Alhusayen
Division of Dermatology, Department of Medicine, University of Toronto, Toronto, ON, Canada
*Correspondence: B.M. Cyrenne. E-mail: benoit.cyrenne@sickkids.ca

References

1 Marzano AV, Cassano N, Genovese G, Moltrasio C, Vena GA. Cutaneous manifestations in patients with COVID-19: a preliminary review of an emerging issue. *Br J Dermatol* 2020; **183**: 431–442.
2 Polack FP, Thomas SJ, Kitchin N *et al*. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med* 2020; **383**: 2603–2615.
3 Drago F, Ciccarese G, Parodi A. Pityriasis rosea and pityriasis rosea-like eruptions: how to distinguish them? *JAAD Case Rep* 2018; **4**: 800–801.
4 Drago F, Ciccarese G, Javor S, Parodi A. Vaccine-induced pityriasis rosea and pityriasis rosea-like eruptions: a review of the literature. *J Eur Acad Dermatol Venereol* 2016; **30**: 544–545.
5 Drago F, Ciccarese G, Rebora A, Parodi A. Human herpesvirus-6, -7, and Epstein-Barr virus reactivation in pityriasis rosea during COVID-19. *J Med Virol* 2021; **93**: 1850–1851.
6 Johansen M, Chisolm SS, Aspey LD, Brahmbhatt M. Pityriasis rosea in otherwise asymptomatic confirmed COVID-19–positive patients: a report of 2 cases. *JAAD Case Rep* 2021; **7**: 93–94.
7 Welsh E, Cardenas-de la Garza JA, Cuellar-Barboza A, Franco-Marquez R, Arvizu-Rivera RI. SARS-CoV-2 spike protein positivity in pityriasis rosea-like and urticaria-like rashes of COVID-19. *Br J Dermatol* 2021: bjd.19833. https://doi.org/10.1111/bjd.19833
8 Chen JF, Chiang CP, Chen YF, Wang WM. Pityriasis rosea following influenza (H1N1) vaccination. *J Chinese Med Assoc* 2011; **74**: 280–282.
9 Papakostas D, Stavropoulos PG, Papafragkaki D, Grigoraki E, Avgerinou G, Antoniou C. An Atypical case of pityriasis rosea gigantea after influenza vaccination. *Case Rep Dermatol* 2014; **6**: 119–123.
10 Ciccarese G, Parodi A, Drago F. SARS-CoV-2 as possible inducer of viral reactivations. *Dermatol Ther*. 2020; **33**: e13878.

DOI: 10.1111/jdv.17342

Cutaneous adverse reactions after m-RNA COVID-19 vaccine: early reports from Northeast Italy

Dear Editor,

We report the first registered cases of cutaneous adverse reactions in Northeast Italy after the m-RNA COVID-19 vaccine