Dear Editor,

Vaccines are biological preparations that enable their recipients to acquire immunity to a specific infectious disease. All vaccines can be associated with cutaneous adverse drug events (ADEs). The new ribonucleic acid (RNA) vaccine type developed by Pfizer-BioNTech was first tested in humans in COVID-19 prevention trials in 2020. This vaccine utilizes lipid nanoparticles, which act as a vector for the embedded mRNA. In a phase III clinical trial, it was found that local reactions at the injection site are the commonest side effect (84.7%), with other adverse reactions including fatigue, headache, muscle ache, chills, joint pain and fever. A recent report described a case of recurrent morbilliform rash that developed 48 h following administration of the Pfizer-BioNTech COVID-19 vaccine on two separate occasions, 21 days apart. We report two patients who presented with cutaneous ADEs following this vaccine.

In brief, both patients were systemically well with no COVID-19 or infection symptoms prior to their COVID-19 vaccinations and the onset of their skin rash. The patients’ clinical characteristics, investigation results and management are presented in Table 1.

| Table 1 Clinical characteristics, investigation results and management for both patients. |
|-----------------------------------------------|
| **Patient 1** | **Patient 2** |
| Age, years | 60 | 75 |
| Sex | Female | Female |
| Ethnicity | White British | White British |
| Comorbidities | Hypothyroidism | Hypertension |
| Dose of Pfizer vaccine | First dose | First dose |
| Vaccine batch number | ER1741 | EL0141 |
| Time to onset of rash following vaccine administration, days | 14 | 2 |
| Duration of skin rash COVID-19 PCR | Rash improved significantly by day 17 (Fig. 1b) Negative | Fully resolved by day 10 (Fig. 2c) Not performed |
| Key investigation results | Negative ANA, ANCA and complement. Normal plasma viscosity and serum electrophoresis. Normal white cell count differentials. Urine microscopy showed red cells $2 \times 10^5/L$. Normal urine albumin/creatinine ratio | Negative ANA, ANCA and complement. Normal plasma viscosity and serum electrophoresis. Normal white cell count differentials. Urine microscopy not performed. Normal urine albumin/creatinine ratio |
| Skin biopsy histology and immunofluorescence | Histology: epidermis showed focal parakeratosis, hyperkeratosis and spongiosis; dermis showed superficial perivascular lymphohistiocytic infiltrate and scattered eosinophils; no definite blood vessel wall fibrinoid necrosis, fibrin thrombi or nuclear dust seen. Negative direct immunofluorescence study | Not performed as the rash had fully resolved by the time the patient first presented to the dermatology team |
| Treatment given | 7-day course of oral prednisolone 30 mg once daily; topical clobetasol 17-propionate 0.05375% w/w (Dermovate) ointment; Cetraban cream as emollient; chlorphenamine 5 mg once daily at night | 5-day course of oral prednisolone 40 mg once daily |

ANA, antinuclear antibody; ANCA, antineutrophil cytoplasmic antibody. "Red blood cell value of $\leq 25$ is not considered significant.
Patient 1 was a 60-year-old woman who developed a rash 2 weeks following vaccination. She presented to Dermatology 2 days later with a widespread symmetrical erythematous and purpuric eruption predominantly affecting her legs (Fig. 1a). Skin biopsies were obtained from the nonpurpuric rash and perilesional skin on her right thigh; histology showed eosinophils and the direct immunofluorescence microscopy result was negative. The rash gradually improved after 7 days of oral prednisolone and topical treatments (Fig. 1b).

Patient 2 was a 75-year-old woman, who developed a confluent erythematous rash on her torso (Fig. 2a) and a symmetrical purpuric rash over the gaiter areas of her legs at day 3; (c) complete resolution of the rash at day 10.
symmetrical purpuric rash over the gaiter areas of her legs (Fig. 2b), 2 days following vaccination. She had no history of lower limb chronic venous insufficiency. The primary care team commenced her on oral prednisolone for 5 days. A skin biopsy was not taken. The rash was fully resolved by day 10 (Fig. 2c). The patient did not experience any ADE following the second Pfizer-BioNTech COVID-19 vaccine.

We report two cases of post-RNA vaccination associated generalized rash with no systemic involvement. To date, the exact mechanism of vaccine-associated cutaneous ADEs remain poorly characterized. It is possible that the whole class of RNA vaccines may share a similar cutaneous ADE profile to that of live and inactivated vaccines. Our patients’ presentation of a purpuric rash on the legs raised the possibility of cutaneous small vessel vasculitis, although the clinical indications were not confirmed by skin biopsy. Vaccine-associated cutaneous vasculitis is a rare event. Bonetto et al. reported influenza vaccination as the vaccine type most likely to trigger vasculitis, particularly the cutaneous vasculitis subtype. Our case series suggest that the mechanism of vaccine-associated cutaneous ADEs may not be dependent upon vaccine uptake by antigen-presenting cells, as is the case for live or inactivated vaccines. Understanding downstream transcriptomics-related events following drug administration (including vaccination) could potentially be useful in the identification of individuals at risk of experiencing ADEs.

M. Lam, M. Egail, A. J. Bedlow and S. Tso
Jephson Dermatology Centre, South Warwickshire NHS Foundation Trust, Warwick, UK
E-mail: simontso@doctors.org.uk
Conflict of interest: the authors declare that they have no conflicts of interest.
ML and ME contributed equally to this work and should be considered joint first authors.
Accepted for publication 1 April 2021

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