Ethical approval

Not required.

Data availability statement

Data are reported in the current study.

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A case of bullous pemphigoid after the SARS-CoV-2 mRNA vaccine

Dear Editor,

A 68-year-old, otherwise healthy, man presented to our dermatology department in late April 2021 with a history of a blistering eruption which commenced 3 days after his first dose of the Pfizer BioNTech COVID-19 vaccine (2 March 2021) and worsened after the second dose given three weeks later. The blisters first appeared over the sternal area and were accompanied by intense, generalized pruritus which started a day before the blisters appeared. His family doctor prescribed acyclovir for a presumed diagnosis of herpes zoster with no improvement and later desloratadine and a 5-day course of 20-mg oral prednisolone. However, the blisters continued to increase in number and erupted over the right side of the chest and upper back particularly after the patient received the second dose of the Pfizer vaccine.

At presentation to dermatology, the patient had several healing crusted areas scattered over the right chest and back but no intact blisters and was prescribed clobetasol propionate ointment and an emollient cream. Routine blood tests, epidermal basal membrane antibodies and prickle cell desmosomes antibodies were normal and negative respectively.

At follow-up, 2 weeks later, there was a recently ruptured blister arising in an area of urticated erythema over his back (Fig 1a, b) and an ulcer situated on the left buccal mucosa (Fig 1c). A biopsy taken from one of the truncal lesions revealed subepidermal blistering associated with a superficial dermal inflammatory infiltrate composed of eosinophils and hemosiderophages. The roof of the bulla consisted of thinned, viable epidermis whilst within the bulla, erythrocytes and scattered inflammatory cells including eosinophils were seen (Fig 1d). Direct immunofluorescence showed linear basal deposition of IgG and C3 (Fig 1e, f). All these findings were in keeping with a diagnosis of bullous pemphigoid (BP). He was advised to continue the previously prescribed topical treatment, and at follow-up 3 months after the first dose of COVID-19 vaccine, he was found to be completely asymptomatic with no new blisters present and only residual post-inflammatory hyperpigmentation present at previously affected sites.

This case is intriguing since to our knowledge it is the first reported case of BP related to the SARS-CoV-2 mRNA vaccine. We acknowledge that a possible differential diagnosis for this case would be epidermolysis bullosa acquisita (EBA). However, the histological features, particularly the eosinophilic-predominant infiltrate, are not typical of EBA and are more in keeping with BP. A large number of cases of BP have been reported following other vaccines including the pneumococcal vaccine[1] and influenza vaccine.[2] However, the pathogenesis is not clear. It has been hypothesized that vaccine-induced inflammation could lead to disruption of the basement membrane architecture with subsequent generation of anti-basement membrane-specific antibodies, and such vaccines may also increase the antigenicity of BP antigens. However, there are no known similarities between the basement membrane protein and the implicated vaccines; therefore, it is unlikely that the vaccine coupled with its respective antibody response is the sole cause of this phenomenon. In fact, it has also been postulated that these vaccines

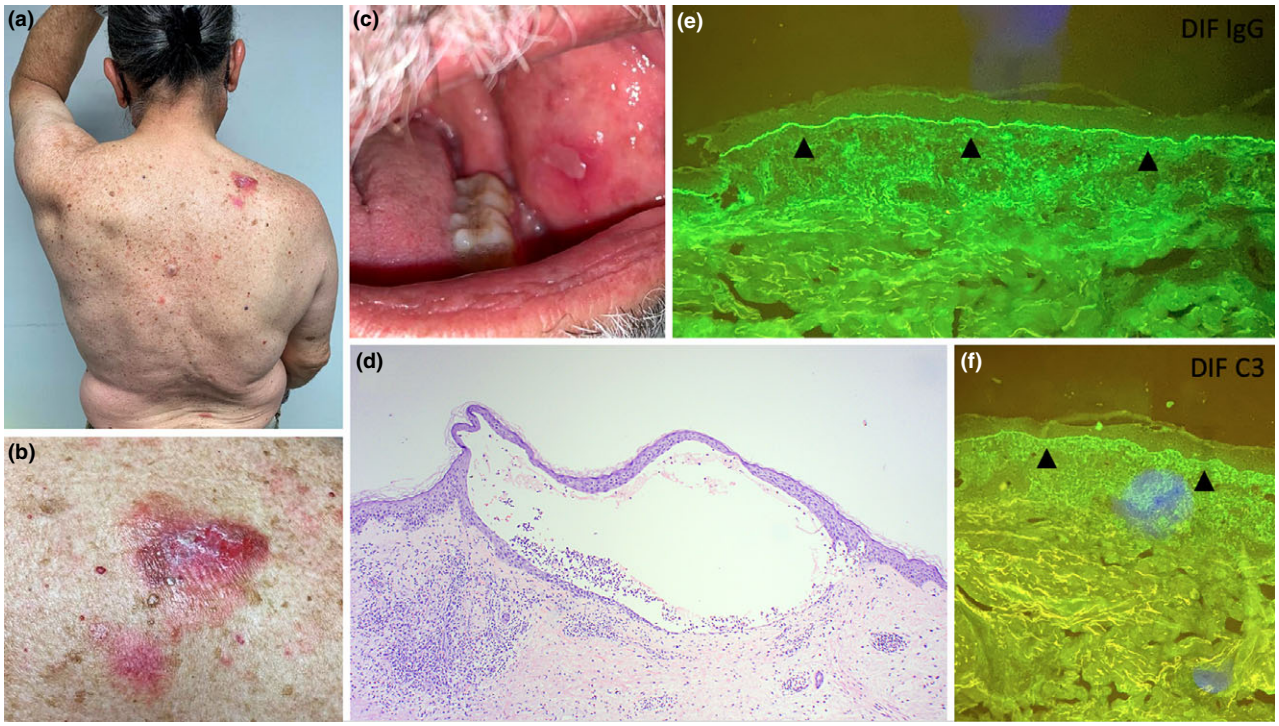

Figure 1 (a, b) Photos taken thirteen weeks after the first dose of the Pfizer COVID-19 vaccine displaying four lesions over the patient's back with a close-up image of one such lesion located over the right upper back. (c) Left buccal ulcer seen at follow-up 2 weeks later. (d) Photomicrograph showing a subepidermal blister roofed by normal epidermis. The blister contains scattered inflammatory cells, and a patchy inflammatory infiltrate is noted in the dermis adjacent to the blister. (H&E stain. Original magnification x 40) (e, f) Linear basal deposition of IgG and C3 noted on direct immunofluorescence (DIF) as indicated by the arrowheads.

may precipitate a heightened immune response in individuals having either subclinical BP or immunological deposition.[2] Interestingly, vaccine-induced-adult BP hasbeen seen mainly in the elderly. This in part may be explained by the phenomenon of immunosenescence which occurs as a result of age-induced thymic atrophy and can lead to autoimmune disease via breakdown of immune tolerance.[1]

On further review of the literature, several articles document other cutaneous manifestations associated with the COVID-19 vaccines (Table 1).[3–9] In a large-scale study by McMahon *et al.*, out of the 414 subjects, no cases of vaccine-induced BP were reported. In fact, the commonest cutaneous manifestations excluding local site reactions were urticaria, morbilliform drug eruptions and erythromelalgia.[10]

Although it is possible that the appearance of BP after COVID vaccination in our patient was coincidental, the onset of symptoms so soon after the first dose, worsening after the second dose, complete resolution within a few weeks with only topical treatment, and no subsequent recurrence suggest a true association in this case.

Acknowledgement

The patient gave written informed consent to the publication of his case details.

Conflict of interest

None.

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Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Table 1 Literature review of the case reports documenting adverse cutaneous reactions as a result of a COVID-19 vaccine[3–9]

Age	Gender	Comorbidities	Vaccine	Presentation	Onset	Treatment	Outcome	Reference
55	Male	Nil of note	Pfizer (1st dose)	Maculopapular rash Face, Trunk, Upper extremities and Thighs	3 h	Topical steroids	Resolution within days Did not take 2nd dose	3
20s	Female	Alopecia	Pfizer (1st dose)	Pityriasis rosea-like eruptions Trunk and Proximal extremities	2 days	Topical steroids	Resolution after 2 weeks	4
40s	Male	Nil of note	Pfizer (2nd dose)	Pityriasis rosea-like eruptions Trunk and Proximal extremities	2 days	Doxycycline and Bilastine	Resolution after 3 weeks	4
60	Male	DM, HTN on Tenegliptin, Metformin, Amlodipine	Unknown (1st dose)	Steven Johnson Syndrome Extensive involvement with oral lesions	3 days	Ciclosporin	Resolution after 7 days Did not take 2nd dose	5
30	Male	Nil of note	Pfizer (both doses)	Pruritic erythematous morbilliform eruption	2 days†	Nil	Resolution after 24 h	6
83	Female	HTN Hypothyroidism Breast cancer on Palbociclib, Letrozole, Vitamin D	Johnson & Johnson (single dose)	Pruritic annular patches with central clearing Trunk and Axilla	2 days	Antihistamines and Topical steroids	Resolution after 2 weeks	7
56	Female	Lichen planus	Pfizer (2nd dose)	Lichen planus Extensive involvement	2 days	Topical steroids	N/A	8
26	Female	Nil of note	Pfizer (both doses)	Fixed drug eruption Near injection site	14 days‡	N/A	N/A	9

Data documented in the study by McMahon *et al.* are excluded in this table.
DM, diabetes mellitus; HTN, hypertension; N/A, not available.
†Cutaneous reaction occurred 2 days after the first dose and recurred 2 days after the second dose.
‡Fixed drug eruption occurred 14 days after the first dose and reappeared 14 days after the second dose.

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Erythema nodosum, zoster duplex and pityriasis rosea as possible cutaneous adverse effects of Oxford–AstraZeneca COVID-19 vaccine: report of three cases from India

Sir,

As a response to the coronavirus disease (COVID-19) pandemic, several vaccines have been developed globally and are being rolled out at a fast pace for public immunization. Drug controller general of India has approved use of Covaxin™ (BBV152, manufactured by Bharat Biotech, Hyderabad, India) and Covishield™ (Oxford–AstraZeneca COVID-19 vaccine, manufactured by Serum Institute of India, Pune, India) for restricted use in emergency situation.[1] We describe three cases of Covishield™ induced minor cutaneous adverse effects.

First case was a 25-year-old woman with complaints of low-grade fever, joint pains and red, and painful nodules over legs and forearm of three days duration. History suggestive of any infection preceding the eruption was denied. She gave history of receiving Covishield 7 days prior to the episode. Cutaneous examination revealed multiple erythematous tender nodules over bilateral shins and forearms (Fig. 1a). Laboratory evaluation revealed elevated inflammatory markers. SARS-Cov-2 was not detected by reverse transcription (RT)-PCR. An extensive workup to rule out underlying aetiologies of erythema nodosum (EN) was negative. Skin biopsy revealed infiltration of dermal and subcutaneous tissue with lymphomononuclear cells and neutrophils, consistent with erythema nodosum (Fig. 1b). Patient was treated with topical mometasone cream and oral paracetamol. Dermatological symptoms had resolved completely at follow-up visit after 2 weeks. No recurrence was observed on receiving second dose after 4 weeks. Infections are the most common cause of EN, and this eruption has been described in association with COVID-19 infection as well.[2,3] EN associated with other vaccines has been rarely reported[4]; however, this is the first report of any COVID-19 vaccine-induced EN to the best of our knowledge.

Second case was a 55-year-old man who presented with first episode of herpes zoster of both T10 dermatomes after COVID-19 vaccination (Fig. 1C). Tzanck smear from the base of blister revealed acantholytic cells and multinucleate giant cells (Fig. 1D). He gave previous history of varicella and had not been vaccinated against herpes zoster. He reported receiving first dose of Covishield 3 days prior to cutaneous eruption. He denied any history of previous unusual infections or family history of any immune defects. Fasting blood sugar level was 95 mg/dL, and HIV test and COVID-19 RT-PCR were negative. He was prescribed oral valcyclovir 1 g thrice a day for 1 week. Resolution of symptoms was noted on follow-up visit after 2 weeks. Immunomodulation by various vaccines has been reported to result in herpes zoster reactivation previously.[5] A recent observational study reported six cases of herpes zoster reactivation in patients with autoimmune rheumatic diseases.[6] Herpes zoster duplex bilateralis has been reported rarely in immunocompetent adults.[7]

Third case was a 24-year-old man with complaints of asymptomatic cutaneous eruption from three days. Examination revealed several well-defined round to oval salmon-coloured papules and plaques up to 3 cm in diameter covered by fine white scales over his trunk, back and axillae (Fig. 2a,b). Patient reported receiving Covishield 24 h prior to onset of cutaneous lesions. Laboratory evaluation was normal, and COVID-19 RT-PCR was negative. Patient did not consent for skin biopsy. In view of characteristic morphology and supportive dermatoscopic findings (Fig. 2c), a diagnosis of pityriasis rosea (PR) was made and he was prescribed topical mometasone cream. Further progression of rash could not be monitored as the patient was lost to follow-up. PR-like rash has been reported previously with COVID-19 infection[8] and other COVID-19 mRNA vaccines.[9] A