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SHORT REPORT

Cutaneous reactions post-COVID-19 vaccination. Case series and literature review

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Abstract

Background: In Saudi Arabia, three approved vaccines against severe acute respiratory syndrome coronavirus 2 (AstraZeneca [AZD1222], Pfizer-BioNTech [BNT162b2] and [Ad26. COV 2-S] Moderna vaccine) have been administered to the population.

Objective: To characterise cutaneous adverse events associated with COVID-19 vaccines.

Methodology: We collected information on 26 patients presented to two secondary health care facilities, over the period extending from mid of December 2020 to the 1st of January 2022 with cutaneous reactions after COVID-19 vaccine administration. Data were descriptively analysed using Statistical Package for the Social Sciences, SPSS 23rd version.

Results: A total of 53.8% of the patients were male; 31% of the patients reported having at least one chronic illness. Reactions were most frequent after the first dose (57.6% of the patients). Messenger RNA-based vaccines were the most frequently noted vaccines associated with the reactions (76.9% of the cases). The most common reactions were cutaneous small-vessel vasculitis (19.2%), interface/lichenoid reactions (19.2%), psoriasis (15.4%), and acute urticaria (11.5%). Only 11.5% patients required admission to the hospital for their clinical presentation.

Conclusion: Most of our patients had mild reactions and were successfully managed with supportive treatments. However, still some patients may experience severe or long-lasting reactions requiring systemic therapies.

KEYWORDS

adenovirus vaccine, coronavirus vaccine, COVID-19 vaccine, cutaneous reactions, mRNA vaccine, side effects

INTRODUCTION

Rare and usually mild adverse events to COVID-19 vaccine, most commonly local injection site reactions, have been reported in clinical trials, and should not dissuade people from getting vaccinated.[1–4] Allergic cutaneous symptoms, such as urticaria and angioedema are transient and rarely linked to anaphylaxis. Herpes zoster and idiopathic thrombocytopenic purpura are rarely significant, although they warrant clinical monitoring in specific individuals.[4] Immune-mediated thrombocytopenia, and cutaneous vasculitis have been reported in the literature as well.[5,6] Most reported cutaneous reactions to COVID-19 are mild and can be managed without medical treatment.[6–10] Although there is a consensus that vaccines are effective and safe, further characterisation of adverse events associated with vaccines is needed for public health and future vaccine developments.

METHODS

We attended in two secondary health care hospitals and outpatient specialist clinics, from mid-December 2020 to the 1st of January 2022, 26 patients with cutaneous reactions who had received one of the available COVID-19 vaccines (AstraZeneca [AZD1222], Pfizer-BioNTech [BNT162b2] or [Ad26. COV 2-S] Moderna vaccine) within 3 months before the reaction. All reported patients were examined and diagnosed by experienced certified dermatologists. Diagnosis was based mainly on clinical features, and skin biopsies were taken if considered necessary.

Data were analysed using Statistical Package for the Social Sciences, SPSS 23rd version. Categorical variables were displayed as frequencies and percentages, while continuous variables were expressed as numbers; minimum, maximum, mean, and standard deviations. The χ^2 test was used to test for an association between categorical variables. Due to the nature of continuous data (nonnormally distributed), the Mann–Whitney U test was also used to test for association. The level of significance was set at a p-value of lower than 0.05.

RESULTS

A total of 26 patients were included in the study. There were 14 (53.8%) males and 12 (46%) females. The age range was 12–63 years, and the mean age was 35.92 ± 13.4. Ten (38%) patients had been previously infected with COVID-19. Eight (31%) patients reported having at least one chronic illness, while eighteen (69%) reported being healthy. Reported illnesses included diabetes mellitus, hypertension, gout, osteoarthritis, goitre, deficiency of G6PDH, uterine fibromatosis, stroke and peripheral arterial disease. Except for psoriasis, the reported clinical disorders were not related to the type of cutaneous reactions developed and are not statistically significant to be correlated with the need for hospital admission secondary to the reaction outcome ($p = 0.91$).

Table 1 summarises the profile of cutaneous manifestations after COVID-19 vaccination. Reactions were more

TABLE 1 Profile of cutaneous reactions post-COVID-19 vaccine ($n = 26$)

	N	%
COVID-19 vaccine dose after which the symptoms appeared		
First	15	57.69
Second	8	30.76
Third	3	11.5
COVID-19 vaccine type		
Adenovirus	6	23
mRNA	20	76.9
Cutaneous reactions		
Cutaneous small-vessel vasculitis	5	19.2
+ Pernio-like lesions	(2/5)	(7.6)
Interface/lichenoid reaction	5	19.2
Eruptive lichen planus	(2/5)	
Erythema multiforme	(2/5)	
Fixed drug eruption	(1/5)	
Psoriasis	4	15.4
Guttate psoriasis	(2/4)	
Psoriasis exacerbation	(1/4)	
Palmoplanter pustular psoriasis	(1/4)	
Acute urticaria	3	11.5
Herpes reactivation	2	7.6
Delayed large local reaction	2	7.6
Local injection site reaction	1	3.8
Erythromelalgia	1	3.8
Erythema nodosum	1	3.8
Pemphigus vulgaris	1	3.8
Dermatomyositis	1	3.8
Interval from receiving vaccine to incidence of symptoms (in days)		
Mean	15.65	
Standard deviation	18	

Abbreviation: mRNA, messenger RNA.

frequently documented after the first dose (57.6%). Messenger RNA (mRNA)-based vaccines were most frequently associated with the reactions, with 76.9% of the cases. Reactions to mRNA-related vaccines developed after the first dose in 50% of cases, while 35% were noticed after the second. On the other hand, 83% and 16.6% of the adenovirus vaccine findings were documented following the first and second doses, respectively ($p = 0.31$). The reactions emerged from 24 h to 60 days after vaccination, with a mean time lapse of 15.65 + 18 days; mRNA vaccines reactions clustered around the first 10 days after administration (Figure 1), whereas adenovirus vaccines showed no definite pattern.

The most frequently observed presentations were cutaneous small-vessel vasculitis five (19.2%), interface/lichenoid reactions five (19.2%), psoriasis four (15.4%), and acute urticaria three (11.5%) (Figures 2 and 3). Cutaneous small-vessel vasculitis was observed more frequently in association with the adenovirus-vectored vaccine. Interface reactions (in the form of lichen planus, erythema multiforme, and fixed drug eruption) developed more frequently after mRNA-based vaccines (three out of five cases). All psoriasis and urticaria cases were noticed after mRNA vaccines. We biopsied only four patients, with histologic diagnoses of Henoch-Schönlein purpura, leukocytoclastic vasculitis, erythema nodosum and pemphigus vulgaris.

Only three (11.5%) patients required admission to the hospital for their reaction, while the other 23 (88.46%) were managed at home. Several factors were tested to investigate an association of the severity of the reactions with hospital admission (Table 2). Most factors, including age of the patient, history of chronic medical illnesses, gender, type of the vaccine provided, timing, and frequency of the doses were statistically non-significant. Female gender appears to be a statistically significant factor increasing the likelihood of hospital admission ($p = 0.046$).

Two of our patients with de novo eruptive lichen planus were managed successfully with a short course of oral steroids. Two patients presented features of urticarial vasculitis and were managed successfully with systemic oral steroids for 3 and 6 weeks, respectively. Only one patient, an adolescent girl who received an mRNA vaccine (Pfizer BioNTech), developed long-lasting severe disease, consisting of Henoch-Schönlein purpura with repeated flare-ups with different triggers, including the second dose of the vaccine; she has required oral steroids and oral azathioprine.

DISCUSSION

We have presented 26 cases of dermatological reactions to COVID-19 vaccination. In contrast to Català et al.,[10] most of our patients were males; although men are overall more likely to be vaccinated, women usually have a more robust antibody response and side effects than men.[11] Moreover, a previous history of COVID-19 infection does not appear to have a statistically significant effect on the reaction severity outcome.[10]

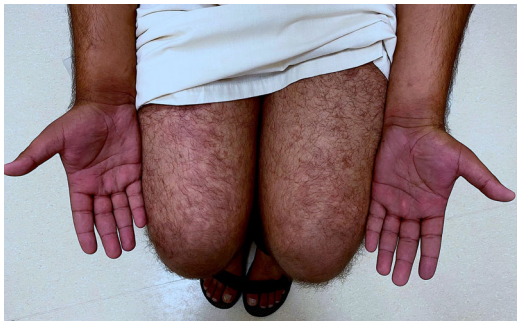

FIGURE 2 Urticarial vasculitis with lesions on the hands and retiform purpuric lesions over the thighs.

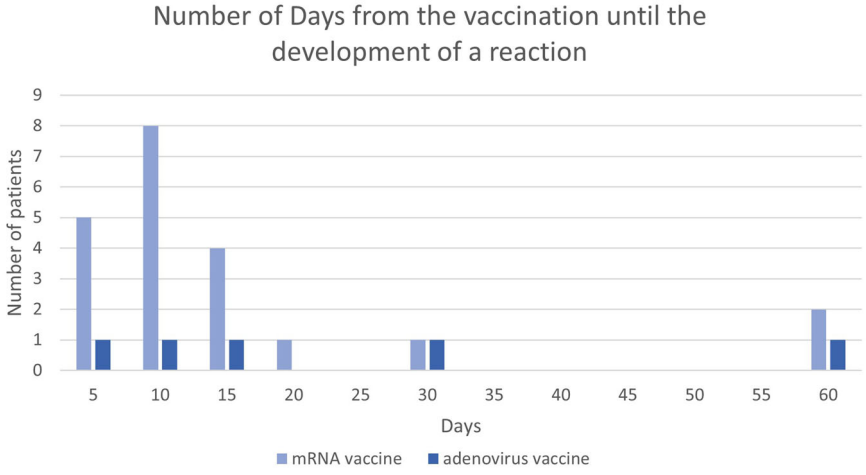

FIGURE 1 Patients cluster around the time line of the reaction development following vaccination.

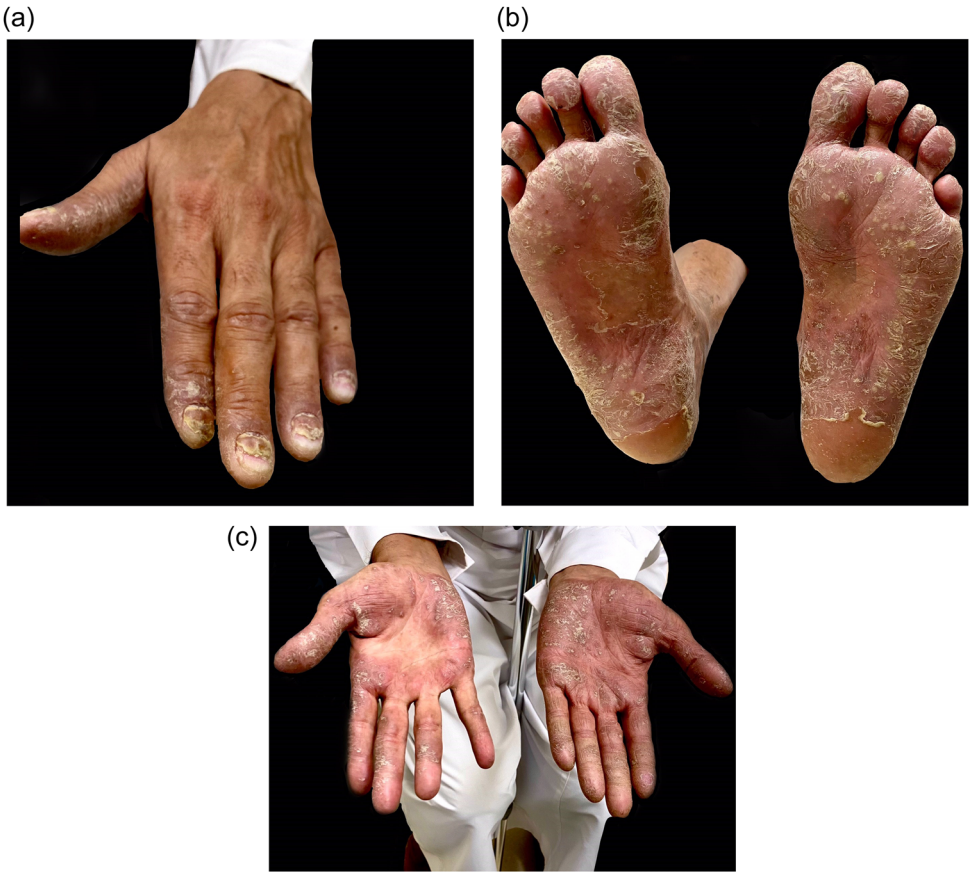

FIGURE 3 (a–c) Palmoplantar pustulosis with severe involvement of the nail units.

Cutaneous small-vessel vasculitis is described particularly with adenovirus vaccine (60%), and more frequently in men after the first dose (80%). Antigen mimicry and the subsequent proinflammatory cascades released are believed to underlie the pathogenesis of immune-complex reactions.[12] While it has been reported that COVID-19 vaccination-associated cutaneous small-vessel vasculitis is self-limited and has a less protracted course than primary cutaneous vasculitis,[6,12] our patients experienced prolonged clinical course and required immunosuppressive treatments.

Rare reactions after COVID-19 vaccinations identified in our study were chilblain-like lesions and erythromelalgia, suggesting the replicative immune response by the vaccine.[13] Erythromelalgia has been reported following several triggers including infections and vaccines,[14] possibly linked to platelet dysfunction and subsequent tissue hypoxia.[15] Aspirin is the recommended choice for erythromelalgia management, followed by antiepileptics.[14]

De novo eruption or exacerbation of a pre-existing cutaneous inflammatory disorder has been reported.[10,13,16] A Th1 response triggered by the vaccine could result in cytokine/chemokine release centrally involved in dermoepidermal junction inflammatory lymphocyte recruitment.[16] Psoriasis induced by the COVID-19 vaccine could be related to a Th17/Th22 predominant milieu in susceptible individuals. Subsequent recruitment of the neutrophils might enhance pustular reactions.[8,16] A similar mechanism has been proposed in COVID-19-induced cutaneous pustular response.[17,18] Our patients had different forms of psoriasis (guttate, chronic plaque exacerbation, and de novo palmoplantar pustular psoriasis), and all of them had received an mRNA vaccine, turned to chronicity, and later required systemic treatment.

Urticaria was the most common adverse event in McMahon et al.[9] registry. The low incidence of acute urticaria in our study could be due to the fact that patients firstly present to emergency or primary care centres rather than to the dermatology clinics.

Delayed localised cutaneous reactions (COVID arm) were frequently observed in trials and after marketing,[9,10,13] particularly with mRNA vaccines. In contrast with local injection site reactions appearing within the first 3 days after vaccination, COVID arm appears after a median of 7 days.[19] Consistent with previous reports,[10] we observed this reaction exclusively in females.

TABLE 2 Factors associated with hospital admission due to the cutaneous reactions post-COVID-19 vaccination

Factor	Hospital admission due to cutaneous manifestation		*p* Value*
	Yes	No	
Gender (*n*, %)			0.046
Male	0	14 (100%)	
Female	3 (25%)	9 (75%)	
Age (mean + standard deviation)	30.67 ± 16.29	36.6 ± 13.27	0.76
Presence of chronic disease (*n*, %)			0.91
Yes	1 (12.5%)	7 (87.5%)	
No	2 (11.11%)	16 (88.88%)	
COVID-19 vaccine dose after which the symptoms appeared (*n*, %)			0.8
First	2 (13.3%)	13 (86.7%)	
Second	1 (12.5%)	7 (87.5%)	
Third	0 (0%)	3 (100%)	
COVID-19 vaccine type (*n*, %)			0.31
Adenovirus	0 (0%)	6 (100%)	
mRNA	3 (15%)	17 (85%)	
History of being infected with COVID-19 (*n*, %)			0.28
Yes	2 (20%)	8 (80%)	
No	1 (6.25%)	15 (93.7%)	
Interval from vaccine to incidence of symptoms (mean + standard deviation)	21.67 ± 8.02	14.87 ± 18.9	0.095

Abbreviation: mRNA, messenger RNA.

*Significant at level 0.05.

Herpes simplex and herpes zoster have been reported repeatedly following COVID-19 infection and vaccination.[10,13] A cell-mediated immune system distraction by either viral or vaccine antigens could activate latent viruses.[10] Interferon-γ release triggered by COVID-19 vaccine can also induce autoimmune or toxic reactions such as dermatomyositis/myositis.[16,20]

Our study has several limitations. First, the study design does not allow calculating the true incidence of severe reactions; indeed, milder reactions are not expected to attend a secondary health care centre. Secondly, skin biopsy is a key tool for the diagnosis; however, only a minority of our cases were biopsied, only when a diagnosis could not be reached clinically. Finally, previously reported and widely known reactions are more likely to draw more attention by patients and primary care physicians after vaccine administration.

In conclusion, while most of our patients were successfully managed with supportive treatment and had a favourable outcome, some others experienced more severe or long-lasting disease requiring systemic therapies. Knowledge of the nature and mechanisms of COVID-19 vaccine reactions and their underlying mechanisms permits an appropriate managing of patients suffering adverse effects of COVID-19 vaccine.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data are available upon journal request.

ETHICS STATEMENT

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

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