

Cutaneous manifestations following COVID-19 vaccination: A report of 25 cases

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Abstract

Various adverse effects particularly cutaneous manifestations associated with different COVID-19 vaccines have been observed in practice. The aim of our study was to evaluate all patients who presented to our tertiary center with skin manifestations following COVID-19 vaccines injection from September to December 2021. All patients with skin manifestation within 30 days or less following COVID-19 vaccination were enrolled in our case-series. All cases included in our study were diagnosed based on clinical and/or histopathological evaluation and all other possible differential diagnoses were ruled out. Twenty-five individuals including 16 (64%) males and 9 (36%) females with the mean age of 47 ± 17.62 years (range 18–91) were enrolled in our study. Twenty-two (88%) patients developed lesions after Sinopharm vaccine injection and 3 (12%) cases manifested lesions after the AstraZeneca vaccine. Six (24%) patients developed new-onset lichen planus (LP) and 1 (4%) patient manifested LP flare-up. Two (8%) individuals developed psoriasis and 1 (4%) case showed psoriasis exacerbation. One (4%) patient developed new-onset pemphigus vulgaris (PV) and 1 (4%) case experienced a flare of PV lesions. One (4%) patient manifested pityriasis lichenoides et varioliformis acuta (PLEVA) flare-up. Other new-onset cases were as follows: toxic epidermal necrolysis (TEN) ($n = 1, 4\%$), bullous pemphigoid (BP) ($n = 2, 8\%$), alopecia areata (AA) ($n = 2, 8\%$), pityriasis rosea ($n = 1, 4\%$), herpes zoster ($n = 1, 4\%$), cutaneous small vessel vasculitis ($n = 1, 4\%$), erythema multiform (EM) and urticaria ($n = 3, 12\%$), and morphea ($n = 1, 4\%$). Physicians should be aware of the possible side effects especially cutaneous manifestations associated with COVID-19 vaccines.

KEYWORDS

astrazeneca, COVID-19, COVID-19 vaccine, side-effect, sinopharm

1 | INTRODUCTION

After the emergence of the COVID-19 pandemic, numerous vaccines against this virus were made available in order to induce immunization in individuals.¹ Various adverse effects particularly cutaneous manifestations associated with different COVID-19 vaccines have been observed in practice.² Local site reactions such as erythema and

induration have been reported to be the most frequent cutaneous adverse effect following COVID-19 vaccination.^{2,3} Furthermore, urticaria, morbilliform, papulovesicular, pityriasis rosea (PR)-like, and purpuric rashes are among other prevalent post-COVID-19 cutaneous reactions.⁴ The post-COVID-19 vaccine cutaneous reactions can be classified into the following categories: local site reactions, type 1 (immediate) hypersensitivity reactions, type 4 (delayed)

hypersensitivity reactions, autoimmune-mediated reactions (such as bullous pemphigoid, lupus erythematosus, vasculitis, vitiligo, thrombotic thrombocytopenic purpura, and alopecia areata), functional angiopathies (such as chilblains-like and perniosis-like lesions), and reactivation of other viral conditions (such as PR, PR-like eruptions, and herpes zoster).⁵

Since the rate of COVID-19 vaccine administration is increasing, it is crucially important to recognize and understand vaccine-related skin reactions. In this regard, we aimed to evaluate all patients who presented to our tertiary center with skin manifestations within 30 days or less following COVID-19 vaccines injection from September to December 2021.

2 | MATERIALS AND METHODS

This study was a case-series analysis conducted in a tertiary referral hospital, Tehran, Iran. All patients with skin manifestation within 30 days or less following COVID-19 vaccination were enrolled in our study. All cases included in our study were diagnosed based on clinical and/or histopathological evaluation and all other possible differential diagnoses were ruled out. Notably, all patients gave informed consent for participating in our study.

3 | RESULTS

Twenty-five individuals with no history of prior SARS-CoV-2 infection including 16 (64%) males and 9 (36%) females with the mean age of 47 ± 17.62 years (range 18–91) were enrolled in our study (Table 1).

Noteworthy that no cases reported initiation of new medications within the last 3 months and all of them denied having a past allergy history.

The interval between the vaccination and skin manifestation was 12.04 ± 6.69 (range 2–27) days.

Notably, 22 (88%) patients developed lesions after Sinopharm vaccine injection and 3 (12%) cases manifested lesions after the AstraZeneca vaccine.

The majority of the patients showed symptoms after the first dose of vaccination ($n = 14$, 56%). Six (24%) cases showed mild symptoms after the first dose that worsened after the second dose. Four (16%) patients developed symptoms after the second dose and one patient developed lesions after the booster dose of vaccine ($n = 1$, 4%).

Six (24%) patients developed new-onset lichen planus (LP) and 1 (4%) patient with a past medical history of LP manifested LP flare-up. Furthermore, two (8%) individuals developed psoriasis and 1 (4%) case with a known history of psoriasis showed psoriasis exacerbation. In addition, 1 (4%) patient with a previous history of pityriasis lichenoides et varioliformis acuta (PLEVA) manifested PLEVA flare-up. One (4%) patient developed new-onset pemphigus vulgaris (PV) and 1 (4%) case experienced a flare of PV lesions.

Other new-onset cases were as follows: toxic epidermal necrolysis (TEN) ($n = 1$, 4%), bullous pemphigoid (BP) ($n = 2$, 8%), alopecia areata (AA) ($n = 2$, 8%), pytriasis rosea ($n = 1$, 4%), herpes zoster ($n = 1$, 4%), cutaneous small vessel vasculitis ($n = 1$, 4%), erythema multiform (EM) and urticaria ($n = 3$, 12%), and morphea ($n = 1$, 4%).

4 | DISCUSSION

Currently, the most common groups of COVID-19 vaccines which are widely being used globally are as follows: (1) Messenger ribonucleic acid (mRNA) vaccines including BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna). (2) Adenoviral vector vaccines including ChAdOx1 nCoV-19 (AstraZeneca) and Ad26.COV2.S (Johnson and Johnson's). (3) Inactivated whole-virus vaccines such as BBIBP-CoV (Sinopharm) and CoronaVac (Sinovac).⁶

All types of COVID-19 vaccines can lead to a wide range of adverse reactions and the most common side effects include local site reactions, which are usually mild and self-limited.⁶ In a study done by Sun et al., delayed-type local reactions were mentioned as the most common cutaneous manifestation following COVID-19 vaccination. Two-thirds of these reactions were related to the Moderna and one-third to the Pfizer-BioNTech vaccines.¹ It is worth mentioning that during the period of our study, no case of local site reaction following COVID-19 vaccination was presented to us. This might be due to fact that our center is a tertiary referral hospital and those complaining of local site reactions after COVID-19 vaccinations generally present to primary or secondary care centers.

In our study, all cases developed cutaneous manifestations following injection of Sinopharm and AstraZeneca vaccines, which might be due to the fact that these two vaccines are among the most commonly used COVID-19 vaccines from our current location, Iran. A study on 867 patients evaluating the cutaneous reactions following COVID-19 vaccination in Iran showed that the majority of individuals manifested symptoms after AstraZeneca, Sinopharm, Sputnik V, and Bharat vaccines, respectively. Furthermore, local site reactions, urticaria, herpes zoster, erythema multiforme-like eruption, exanthematous and petechiae purpuric rashes were among the frequently reported adverse effects following AstraZeneca and Sinopharm vaccines.²

Molecular mimicry between the vaccine-induced proteins of SARS-CoV-2 and human components might result in the production of pathological autoantibodies causing autoimmunity.⁷ Accordingly, cases of new-onset or trigger of the autoimmune diseases were observed in our study.

Previous studies have shown that psoriasis patients are more inclined to receive the COVID-19 vaccine, as compared to control groups who have other skin diseases and are on immunosuppressive medication.⁸ Significant worsening of pre-existing psoriasis and new-onset, notably guttate, have been reported following AstraZeneca, Moderna, and Pfizer vaccines.⁹ In our study, all three cases of psoriasis manifested pruritic plaques following the Sinopharm vaccine

TABLE 1 Characteristics of the patients

Case number	Sex	Age	Past medical or allergic history	Past drug history	Vaccine name	First, second, or booster dose	Skin manifestation following vaccination	Symptom	Interval days between vaccination and symptom presentation	Lab, imaging, and histopathologic findings	Treatment	Outcome	Follow ups
Lichen planus													
1	Female	45	Hypertension	Metoral 50 mg ½ Table BD since 3 months before vaccine injection, Losartan 25 BD since 3 months before vaccine injection	Sinopharm	First	Violaceous papules located on arm and forearms, and ankle	Mild pruritus	14 days	AST:83,ALT:206, ALP:216,	Topical corticosteroid	Significant improvement	Post inflammatory hyperpigmentation (PIH) in Forearm and ankle observed at the follow up session 3 months after the first dose injection.
2	Male	40	None	None	Sinopharm	Mild symptoms after the first dose that worsened after the second dose.	Violaceous papules located on wrist and forearms	Mild pruritus	10 days	N/A	Topical corticosteroid	Significant improvement	N/A
3	Male	38	Lichen planus	Topical corticosteroid	Sinopharm	Mild symptoms after the first dose that worsened after the second dose	Violaceous papules located on arm and forearms	Moderate pruritus	21 days	N/A	Topical corticosteroid, calcineurin inhibitor	Significant improvement	PIH in Forearm, arm observed at the follow up session 3 months
4	Male	45	None	None	Sinopharm	Mild symptoms after the first dose that worsened after the second dose.	Generalized violaceous papules more dominantly located on forearms and chest.	Pruritus	7 days	N/A	Topical corticosteroid	Significant improvement	N/A
5	Male	45	None	None	AstraZeneca	First	Generalized violaceous papules dominantly acral	Pruritus	7 days	N/A	Systemic prednisolone	Significant improvement	N/A
6	Female	49	None	None	Sinopharm	First	Generalized violaceous papules dominantly acral	Pruritus	10 days	N/A	N/A	Significant improvement	N/A
7	Male	32	None	None	Sinopharm	Second	Generalized violaceous papules and plaques more dominantly involved extremities	Pruritus	10 days	N/A	Oral prednisolone	Significant improvement	N/A
Psoriasis													
8	Female	18	Psoriasis	Topical corticosteroid	Sinopharm	Second	Generalized scaly plaques	Pruritus	7 days	N/A	Topical corticosteroid, emollient, Calcipotriol	Mild improvement	Methotrexate was prescribed
9	Male	34	Chronic urticaria	Cetirizine	Sinopharm	Mild symptoms after the first dose that worsened after the second dose.	Generalized erythematous scaly papules, urticaria	Pruritus	9 days	N/A	Topical corticosteroid	Significant improvement	N/A
10	Male	50	Arthritis	Sulfasalazine, methotrexate	Sinopharm	Mild symptoms after the first dose that worsened after the second dose.	Generalized erythematous scaly plaques	Pruritus	4 days after the first dose, Exacerbation 6 days after the second dose	N/A	Adalimumab	Significant improvement	N/A

(Continues)

TABLE 1 (Continued)

Case number	Sex	Age	Past medical or allergic history	Past drug history	Vaccine name	First, second, or booster dose	Skin manifestation following vaccination	Symptom	Interval days between vaccination and symptom presentation	Lab, imaging, and histopathologic findings	Treatment	Outcome	Follow ups
Toxic epidermal necrolysis (TEN)													
11	Male	71	none	None	Sinopharm	First	generalized erythema, necrosis, and bullous detachment of the epidermis and mucous membranes with positive nikolsky sign	Pain, pruritus, fever	10 days	N/A	Intravenous dexamethasone	Significant improvement	N/A
Pemphigus vulgaris													
12	Female	28	Pemphigus vulgaris	Prednisolone	Sinopharm	First	Exacerbation of the underlying disease (pemphigus vulgaris) Mucocutaneous vesiculobullous erosions	None	14 days	N/A	Prednisolone, rituximab	Significant improvement	PIH
13	Female	30	None	None	Sinopharm	First	Oral and mucosal vesiculobullous erosions	Pain	16 days	NL	Prednisolone, Rituximab	Significant improvement	N/A
Bullous pemphigoid													
14	Female	85	None	None	Sinopharm	First	Generalized cutaneous blisters and ulcers	Pruritus	20 days	N/A	Topical clobetasol and oral doxycycline	Significant improvement	N/A
15	Male	91	None	None	Sinopharm	First	Mucocutaneous ulcers	Pruritus	19 days	N/A	Topical Clobetasol, Rituximab	Significant improvement	N/A
Alopecia areata													
16	Male	74	Fatty liver	None	Sinopharm	Second	Scalp and beard area alopecia	None	2 days	N/A	Intralesional Corticosteroid injection	Significant improvement	N/A
17	Male	37	None	None	Sinopharm	Mild symptoms after the first dose that worsened after the second dose.	Beard area after the first dose that progressed into scalp and eyebrow alopecia	None	6 days	N/A	Intralesional Corticosteroid injection	Significant improvement	N/A
Pityriasis lichenoides et varioliformis acuta (PLEVA)													
18	Male	54	PLEVA	None	Sinopharm	First dose	PLEVA flare characterized by generalized scaly plaques	None	27 days	Histopathologic study showed epidermal acanthosis, spongiosis, parakeratosis, dermal lymphohistiocytic infiltrate, lymphocytic exocytosis	None	Significant improvement	N/A

TABLE 1 (Continued)

Case number	Sex	Age	45	None	Past medical or allergic history	Past drug history	Vaccine name	First, second, or booster dose	Skin manifestation following vaccination	Symptom	Interval days between vaccination and symptom presentation	Lab, imaging, and histopathologic findings	Treatment	Outcome	Follow ups
Cutaneous small vessel cutaneous vasculitis															
19	male	45	None	None		None	Sinopharm	First dose	Papular lesions on upper and lower limbs	Pruritus	2 days	Histopathological study showed vascular damage, fibrinoid necrosis, red blood cell extravasation, nuclear dust and neutrophilic infiltration as well as few eosinophils compatible with small vessel cutaneous vasculitis. Sonographic evaluation showed idiopathic liver cirrhosis, normal liver function test	Prednisolone	Significant improvement	PIH in the 3 months follow up.
Pyrtiasis rosea															
20	Male	56	Hyper tension, diabetes mellitus	Insulin			Sinopharm	Booster	Annular lesions on trunk, with trailing collarete scale	Pruritus	14 days	N/A	Topical corticosteroid	Significant improvement	N/A
Herpes zoster															
21	Female	60	None	None			Sinopharm	First	Multiple vesicles	Pain	6 days	N/A	Valacyclovir	Signifi cant improve ment	PIH
Urticaria and erythema multiform															
22	Female	50	Psoriasis	Topical corticosteroid			Sinopharm	First	Target lesions located on the trunk	Mild pruritus	25 days	N/A	Prednisolone	Signifi cant improve ment	N/A
23	Male	31	None	None			Sinopharm	Second	Generalized urticaria	Pruritus	11 days	N/A	Fexofenadine hydrochloride, cetirizine hydrochloride	Signifi cant improve ment	N/A
24	Female	32	None	None			AstraZeneca	First	Urticarial and targetoid lesions	Fever,	20 days	WBC:10100 AST:79 ALT:139 ESR:49 CRP: negative	Prednisolone, topical clobetasol	Significant improvement	None
Morphea															
25	Female	35	Hyperlipidemia, diabetes	Atorvastatin, mefformin			AstraZeneca	First	Generalized sclerotic lesions	Pruritus	10 days	ESR:51 CRP:5	Prednisolone, Methotrexate	Mild improvement	Follow up

Abbreviations: PCSM-TCL, primary cutaneous CD4-positive small/medium T-cell lymphoma; PIH, post-inflammatory hyperpigmentation; PLEVA, pityriasis lichenoides et varioliformis acuta; TEN, toxic epidermal necrolysis.



FIGURE 1 (A–C) A 34-year-old male patient with a past medical history of psoriasis and chronic urticaria controlled with cetirizine experienced generalized erythematous scaly papules and urticarial lesions following Sinopharm vaccine

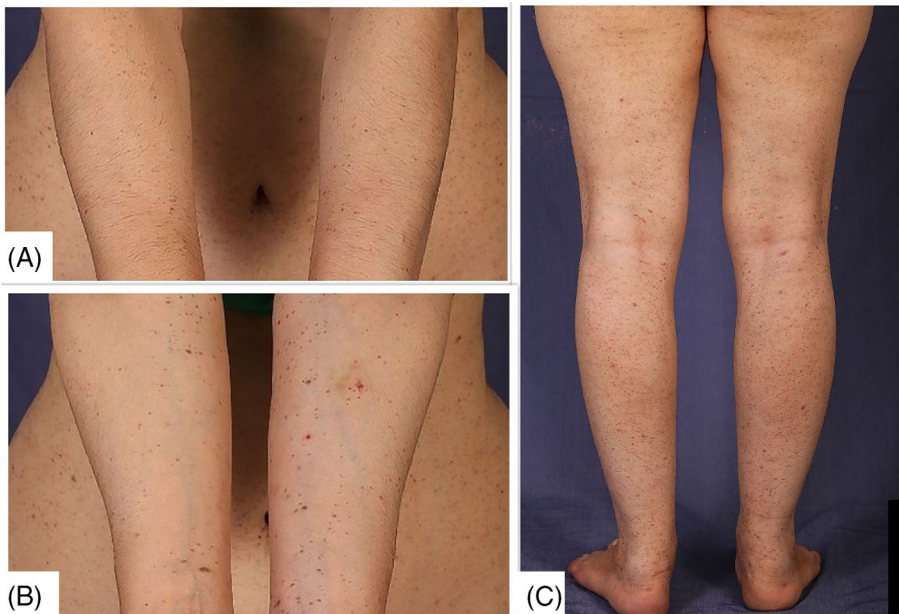


FIGURE 2 (A–C) A 49-year-old female without any past medical history that developed lichen planus following Sinopharm vaccine

(Figure 1). There is some evidence that systemic treatment can protect against vaccine-mediated flares of psoriasis, whereas patients receiving no treatment or only topical treatment are likely to activate an inflammatory process resulting in new and often extensive lesions.⁹ The only case of psoriasis flare-up in our study was a female patient who was under therapy with a topical corticosteroid that experienced a psoriasis exacerbation 7 days following the second dose of Sinopharm vaccine. Furthermore, cases of acute generalized pustular psoriasis (AGPP) have been observed 5 days after receiving the first dose of Pfizer vaccine¹⁰ and also, 4 days after getting the first dose of CoronaVac vaccine.¹¹

Similar to the findings of our study (Figure 2), cases of new-onset LP or exacerbation of the previous condition following Sinopharm and AstraZeneca vaccines have been reported in the literature.¹² It has been postulated that vaccines can start the inflammatory cascade by cytotoxic CD8 T-lymphocytes which lead to keratinocytes basal apoptosis and subsequent releasing of the cytokines such as IFN- γ and IL-5 causing LP eruptions.¹² In this regard, Diab et al, described a case of lichenplanopilaris (LPP) relapse and development of lichen planus in a 60-year-old woman 14 days after the second dose of AstraZeneca vaccine.¹² Moreover, Sharda et al. reported a case of oral lichen planus 14 days after COVID-19 vaccination.¹³

Previous reports of new-onset AA following Pfizer, AstraZeneca, and Moderna vaccines suggest that adjuvants and vaccine antigens may trigger T cell-mediated immune responses, which could lead to AA in genetically susceptible individuals.^{7,14} In this regard, in our study, we observed two cases of AA after the Sinopharm vaccine (Figure 3).

Previous studies have suggested that Moderna, Pfizer, and AstraZeneca vaccines can trigger autoimmune bullous diseases (AIBDs). In this study, we observed BP and PV cases after getting the first dose

of Sinopharms (Figure 4).^{15,16} It has been suggested that COVID-19 vaccines contribute to the production of cytokines like IL-4, IL-17, and IL-21 that play a critical role in autoimmune disorders such as pemphigus, especially in the early stages.¹⁷

In this study, we observed a case of pemphigus flare up. Our patient was in complete remission of pemphigus for the past 3 years. She had a history of pemphigus in the past for which she had received prednisolone but the medication was discontinued 3 years ago. She had not taken any medication for the last 3 years. After the first dose

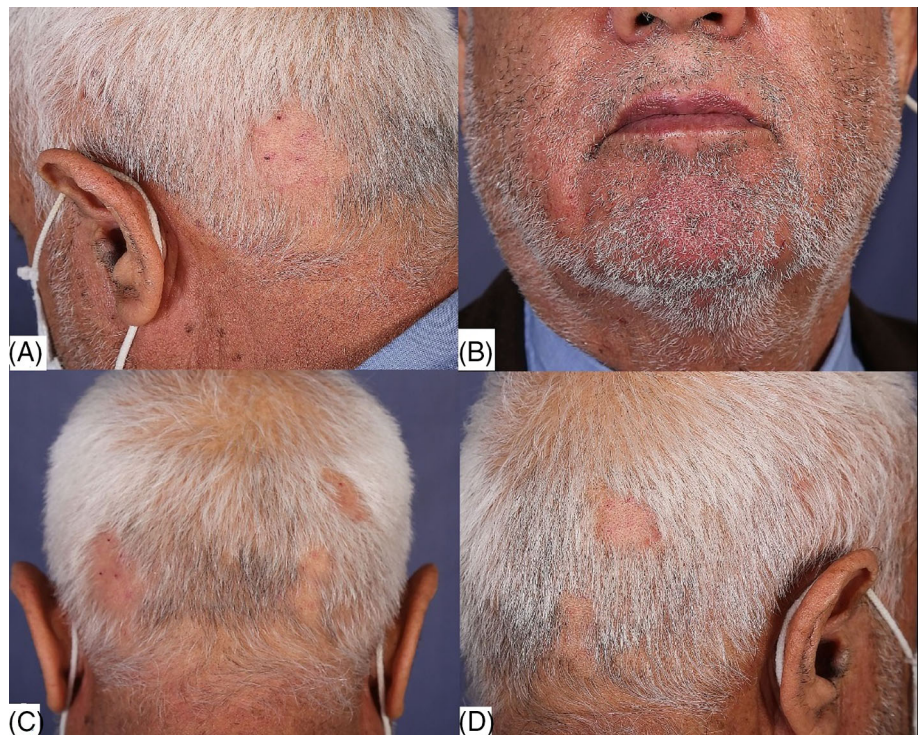


FIGURE 3 (A–D) A 74-year-old male with scalp and beard area alopecia following Sinopharm vaccine

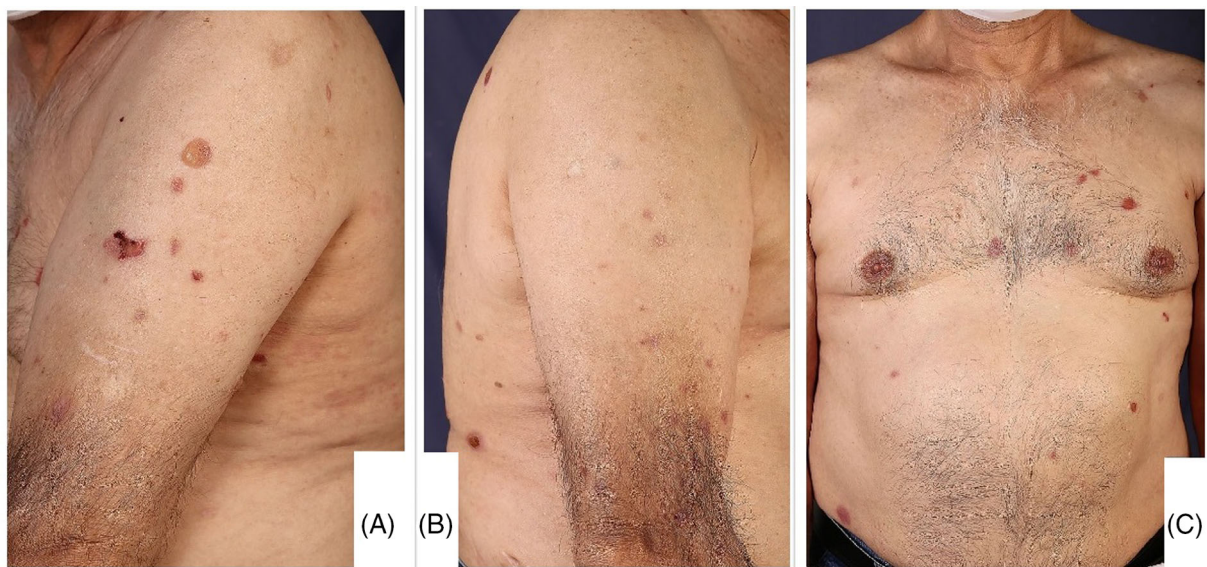


FIGURE 4 (A–C) A 85-year-old male with bullous pemphigoid after Sinopharm vaccine

of Sinopharm vaccine, she experienced pemphigus flare up and she was managed with 4 mg dexamethasone three times a day.

In this study, we observed a case of PLEVA 27 days after the first dose of the Sinopharm vaccine. Similar cases of PLEVA have also been reported in the literature following 9 and 5 days after the first and second dose of Pfizer, respectively.¹⁸

In addition, a case of generalized morphea was observed in our study in a female patient 10 days after the AstraZeneca vaccine. In this regard, Metin et al. reported a case of morphea following the administration of the COVID-19 mRNA vaccine.¹⁹

In our study, we observed cases with urticarial and EM-like lesions which were managed with corticosteroids and anti-histamines. Similar lesions have been observed following vaccination with Pfizer, Moderna, and CoronaVac vaccine.^{20,21}

Furthermore, we observed one case of TEN following the first dose of vaccination with Sinopharm vaccine which was managed with corticosteroids. TEN is a delayed-type four-hypersensitivity reaction that is considered as a medical emergency requiring immediate medical intervention. Also, another case of TEN was reported in a 49-year-old woman with no previous medical history 1 week after getting the first dose of Pfizer which was managed by etanercept.²²

As observed in our study, activation of viral conditions such as PR and Varicella zoster virus following COVID-19 vaccines have been reported previously. In a study done by Mc Mahon et al. on 414 skin reactions to the COVID-19 mRNA vaccines including Moderna and Pfizer, herpes zoster, herpes simplex, and PR-like reactions (PR-LE) were reported in 1 case after the first dose of Moderna, 2 cases following the first dose of Pfizer and 1 report after the second dose of Pfizer, respectively.²¹

Cutaneous reactions to COVID vaccines can happen following first, second, or booster doses.²³ In our study, we observed a case of

cutaneous small vessel vasculitis 2 days after the first dose of Sinopharm vaccine (Figure 5). In this regard, another case of cutaneous small vessel vasculitis was reported by Kar BR et al. following administration of COVAXIN.²⁴

Previous studies have shown the association of anti-hypertensive medications such as beta-blockers with LP and LP-like eruptions.²⁵⁻²⁷ In this study, we observed a case of new-onset LP in a patient with the past medical history of hypertension. She had been taking antihypertensive medications including metoral and losartan since 6 months before COVID-19 vaccination. During the past 6 months of therapy with metoral and losartan, she did not develop any cutaneous lesions. She developed LP lesions 2 weeks after getting her first dose of Sinopharm vaccine. Accordingly, we diagnosed this patient with vaccine-related LP. As a result of these time intervals, we did not relate her LP to the antihypertensive medications she was taking. It is worth mentioning that a definite judgment cannot be made and these two risk factors might have caused the disease together and more studies are recommended in this field.

In our study, we observed that most cases were new-onset diseases and a minority were flare-ups of an underlying disease. In a study done by Avallone et al., new-onset diseases were more frequent than flares of pre-existing conditions.²⁸ In literature, both exacerbation and new-onset cutaneous diseases following COVID-19 vaccines have been reported. Currently, there exists no accurate data regarding comparing the frequency of new-onset and flare-ups of cutaneous diseases after COVID-19 vaccination in exact number. Hence, a definite judgment cannot be made and more studies are recommended in this field.

It is worth mentioning that six patients in our study developed mild symptoms with the first dose of vaccine that worsened after the second dose. The results of our study suggest that patients with a



FIGURE 5 (A-C) A 45-year-old male without any past medical history that developed cutaneous small vessel vasculitis after Sinopharm vaccine

history of reaction following COVID-19 vaccines are generally at a higher risk of developing adverse reactions following administration of second or booster doses. Based on our recommendation, individuals with pre-existing dermatological conditions should be informed about the possible exacerbation of their disease after the COVID-19 vaccination.

However, there exists no strict contradiction for injecting the following doses of COVID-19 vaccines in patients with a previous history of adverse reactions. Also, it has been suggested that patients with a history of reactions with the first dose of the COVID-19 vaccine should not defer injecting the following doses themselves and they should consult with a specialist for injecting the next doses.^{20,24}

5 | CONCLUSION

While rare, the immune dysregulation caused by COVID-19 vaccines can subsequently cause a new-onset skin manifestation or worsen an underlying condition.

Our study suggests 11 different categories of skin manifestations within 30 days or less following vaccination with Sinopharm and AstraZeneca vaccines. The interval between the vaccination and skin manifestation was 12 days. Most patients showed reactions after administration of the first dose of the vaccine. Moreover, some cases showed mild symptoms after the first dose of vaccine that worsened after the second dose.

Mass vaccination against COVID-19 is the key to stopping the current pandemic and physicians should be aware of the possible side effects especially cutaneous manifestations associated with COVID-19 vaccines.²⁵

AUTHOR CONTRIBUTIONS

All authors contributed to the preparation and finalization of this article. **Safoura Shakoei**: Contributed in writing the article and study design, contributed in literature review, contributed in final editing. **Yasamin Kalantari**: Contributed in writing the article and study design, contributed in final editing. **Maryam Nasimi**: Contributed in writing the article and study design. **Nasim Mazloumi Toutouchi**: Contributed in literature review, contributed in final editing. **Mahshid Sadat Ansari**: Contributed in literature review, contributed in final editing. **Zahra Razavi**: Contributed in writing the article and study design. **Ifa Etesami**: Contributed in writing the article and study design, contributed in final editing.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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