

Cutaneous Adverse Reactions after Administration of Covishield Vaccine in a Tertiary Care Hospital in Western Uttar Pradesh: A Series of Cases

Pihu Sethi¹, Kriti Maheshwari², Bhuvan Adhlakha³, Shivani Kalhan⁴, Rakesh Kumar Gupta⁵

¹Assistant Professor, Department of Dermatology, Venereology and Leprosy, Government Institute of Medical Sciences, Greater Noida, Uttar Pradesh, India.

²Senior Resident, Department of Dermatology, Venereology and Leprosy, Government Institute of Medical Sciences, Greater Noida, Uttar Pradesh, India.

³Assistant Professor, Department of Pathology, Government Institute of Medical Sciences, Greater Noida, Uttar Pradesh, India.

⁴Professor, Department of Pathology, Government Institute of Medical Sciences, Greater Noida, Uttar Pradesh, India.

⁵Professor, Department of Paediatrics, Government Institute of Medical Sciences, Greater Noida, Uttar Pradesh, India.

Received: 17-09-2022 / Revised: 21-10-2022 / Accepted: 05-11-2022

Corresponding author: Dr Pihu Sethi

Conflict of interest: Nil

Abstract

COVID-19 is a recently discovered highly communicable disease caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) and its variants. The sudden emergence of the COVID 19 pandemic and its impact on global health meant that the development of effective and safe vaccines was crucial for this new lethal disease as vaccination always plays an essential role in the advancement of global health. So far, there are three main types of COVID-19 vaccines in use around the world: mRNA-based vaccines, adenoviral vector vaccines, and inactivated whole-virus vaccines. Since the introduction of vaccines for the COVID-19 disease, various reports of a spectrum of mucocutaneous side effects have surfaced. With the aid of this case series we would like to highlight the different types of cutaneous adverse effects that were observed post vaccination with the COVISHIELD™ vaccine by the department of Dermatology at our institution.

Keywords: COVISHIELD vaccine, Photoallergic dermatitis, Pompholyx, Vaccine, Urticaria, Drug reaction, COVID-19

This is an Open Access article that uses a fund-ing model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

COVID-19 is a recently discovered highly communicable disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and its variants [1]. At the initial stage of the pandemic, the outcome of

COVID – 19 was highly unpredictable and associated with a high mortality rate [2]. Due to the deficiency of effective therapeutic modalities for the disease, an urgent need for vaccination against COVID – 19 was

identified across the globe. Due to the emerging pandemic, vaccinations like COVISHIELD™ were granted approval for emergency use in India in early January 2021.

COVISHIELD™ is a ChAdOx1 nCoV-19 Corona Virus Vaccine encoding the SARS-CoV-2 Spike (S) glycoprotein that is produced in genetically modified human embryonic kidney (HEK) 293 cells. The vaccine is injected intramuscularly with a minimum interval of 4 weeks [3]. As per the Serum institute of India Pvt. Ltd COVISHIELD™ Vaccine includes the following ingredients:

L-Histidine, L-Histidine hydrochloride monohydrate, Magnesium chloride hexahydrate, Polysorbate 80, Ethanol, Sucrose, Sodium chloride, Disodium edetate dihydrate (EDTA), Water for injection. Of the above ingredients, Polysorbate 80 has been reported to have developed hyperhidrosis, pruritus and rash [4].

During the initial phase, only the population above 45 years of age was being administered with the vaccine in India, which was followed by vaccination of individuals aged 18 to 45 years. In this case series we are describing the spectrum of cutaneous adverse effects observed by the outpatient department of Dermatology at our institution.

Case Presentations

Patient 1: Photoallergic Dermatitis

A 40-year-old male who received the first dose of COVISHIELD™ vaccine presented with itchy cutaneous eruptions over photo exposed areas that developed over 1-2 days after receiving the vaccination. The patient had a construction business and gave history of sun exposure for approximately 7 hours after receiving the vaccination. There was no history of any medications prior to onset of lesions, any co morbidities, photosensitivity

or similar lesions in the past. The distribution of the lesions was remarkably over the photo-exposed sites with well-defined margins adjacent to photo-protected sites.

On examination, there was diffuse erythema with scaling over malar area of the face. Erythematous plaques with scaling were present over the neck and upper chest, upper portion of the back of the neck, and extensor surfaces of bilateral forearms (Figure 1, Figure 2, Figure 3, Figure 4). Mucocutaneous examination of other sites, general physical and systemic examinations were unremarkable. Blood picture demonstrated total leukocyte counts to be 10,000/microliter with eosinophilia.

The test for antinuclear antibodies (ANA) was negative. Liver and kidney function tests and urine routine examination was within normal range. Biopsy from skin was done for histopathological examination which revealed epidermis with parakeratosis, focal acanthosis and spongiosis at places; dermis showed mild edema with chronic inflammatory cell infiltrate (Figure 5, Figure 6). The patient denied a photopatch test post recovery. Based on the history, clinical presentation, careful examination and distribution pattern, and histopathological findings of the lesions, a diagnosis of photoallergic dermatitis was made.

The patient was managed with oral cetirizine 10 mg and mometasone 0.1% lotion twice daily. Strict photoprotection was also advised. Subsequent dermatological evaluation revealed post inflammatory hyperpigmentation with few areas of eczematous dermatitis persisting after treatment for 15 days.

The patient was contacted telephonically after 5 months of presentation and he gave history of not taking the 2nd dose of the vaccine due to fear recurrence.



Figure 1: Distribution of the lesions over photo-exposed areas



Figure 2: Diffuse erythema with scaling over malar area of face. Well defined erythematous plaques over neck and upper chest



Figure 3: Diffuse erythema with scaling over malar area of face – Right side



Figure 4: Diffuse erythema with scaling over malar area of face – Left side

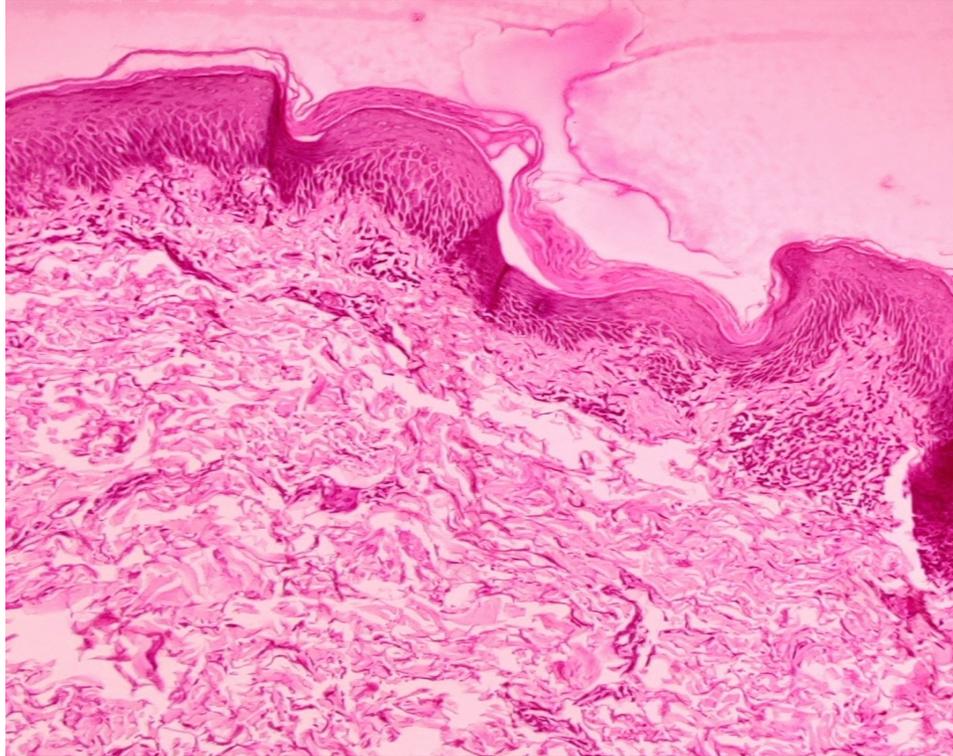


Figure 5: Biopsy showing epidermis with parakeratosis, focal acanthosis (H&E 10x)

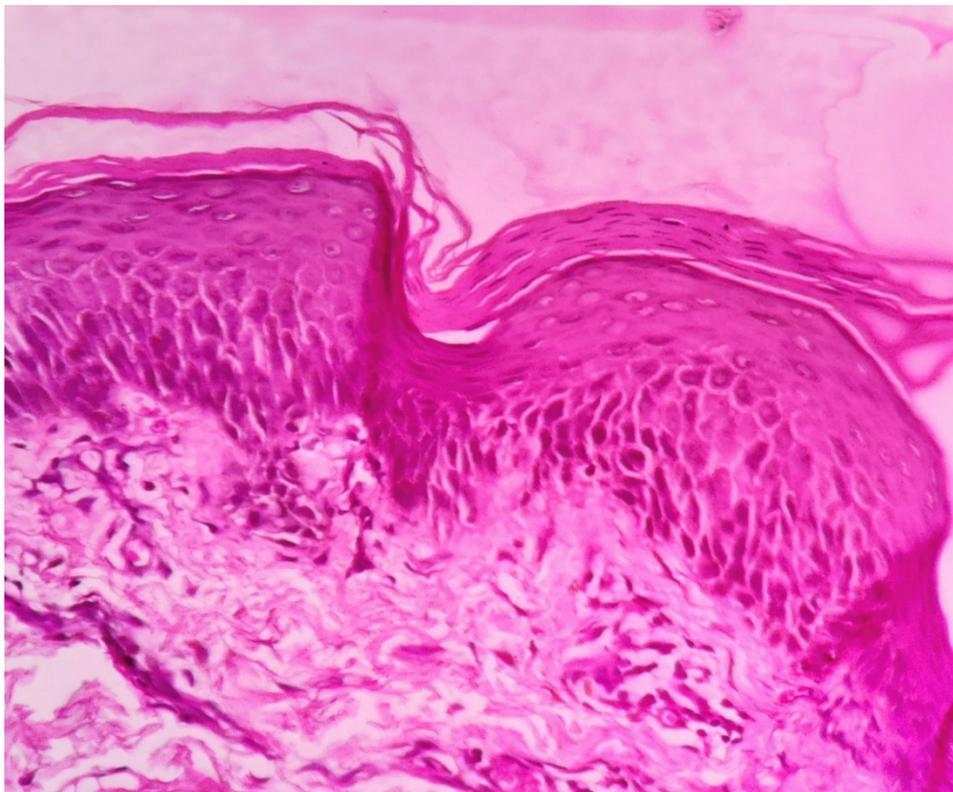


Figure 6: Biopsy showing epidermis with parakeratosis, focal acanthosis and spongiosis at places; dermis showing mild edema with chronic inflammatory cell infiltrate (H&E 40x)

Patient 2: Herpes Simplex Reactivation

A 32-year-old female presented with complaints of painful fluid filled lesions on chin that developed 1 day after receiving 1st dose of COVISHIELD™ vaccine. Patient gave history of similar lesions around lips 3 years back which resolved after treatment. There was no history of fever, stress, excessive sun exposure prior to onset on lesions. No history of any other cutaneous disorders, comorbidities or any immunosuppressive condition. On examination, multiple, grouped vesicles and pustules were present on the chin (Figure 7). Tzanck smear studied showed multinucleate giant cells with few acantholytic cells (Figure 8). A diagnosis of herpes simplex was made on the basis of classical clinical presentation and tzanck smear. Patient was treated with tablet acyclovir 400 mg thrice daily for 14 days, however was lost to follow up.



Figure 7: Grouped vesicles with turbid fluid and surrounding erythema over chin

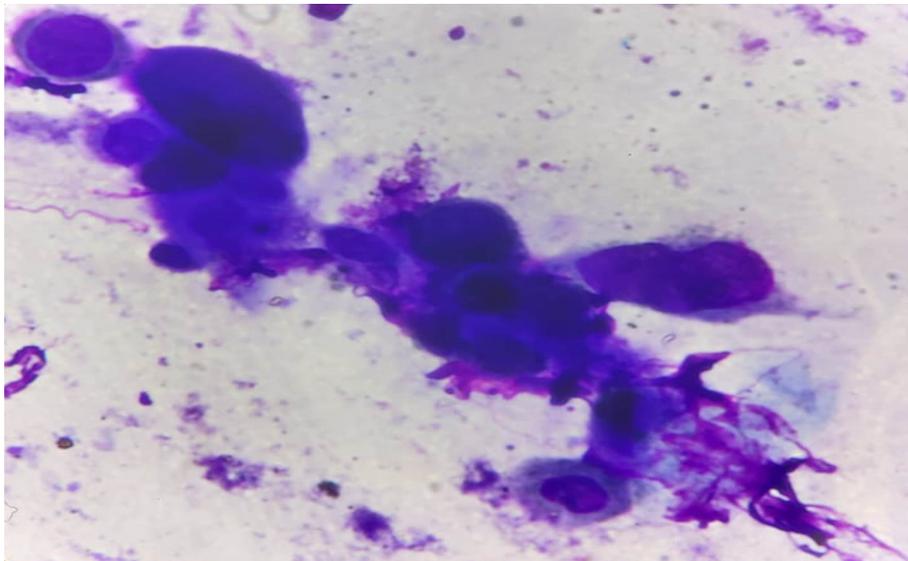


Figure 8: Tzanck smear showing multinucleate giant cells with singly scattered acantholytic cells (40x)

Patient 3: Pompholyx

Patient was a 32 year old male who presented with pruritic lesions on both hands 2 days after receiving the second dose of COVISHIELD™ vaccine. There was no history of any contact with irritants or allergens like soluble oils, household chemicals, fragrances, cobalt, nickel etc prior to onset of the lesions, atopy, similar lesions in the past or post 1st dose of the vaccine, any oral medications or any other co-morbidities.

The lesions were tense, deep-seated crops of "sago-like" vesicles seen on bilateral palms and were intensely pruritic (Figure 9). Based on the clinical history and examination a diagnosis of pompholyx was made. Patient was treated with emollient and clobetasol propionate 0.05% cream twice daily along with tab cetirizine 10 mg daily for 14 days. Patient was also advised to maintain strict protective measures to prevent aggravation of the condition. The lesions resolved completely on treatment.



Figure 9: Deep seated vesicles over palms

Patients 4, 5 and 6: Urticaria

Patient 4 was a 25-year-old male who presented with complaints of intensely pruritic rash all over the body 1 hour after 1st dose of COVISHIELD™ vaccine. The lesions were also accompanied by headache and malaise. There was no history suggestive of angioedema, difficulty in breathing, skin disease, reactions after other vaccinations or medications or similar lesions due to any

triggers. On examination, there were erythematous, urticarial wheals all over the body mainly over extremities and trunk (Figure 10). The patient was treated with tablet cetirizine 10mg twice daily for 7 days along with calamine lotion. Lesions resolved within 24 hours of initiating treatment. The patient was contacted telephonically after 5 months when he confirmed he had taken the 2nd dose of the vaccine and did not develop such lesions again.



Figure 10: Wheals present over extremities and trunk

Patient 5 was a 28-year-old male who presented with complaints of intensely pruritic rash all over the body 6 hours after 1st dose of COVISHIELD™ vaccine. There was no history suggestive of angioedema, difficulty in breathing, fever, headache, myalgia, skin disease, reactions after other vaccinations or medications or similar lesions due to any triggers. On examination, there were erythematous, urticarial wheals all over the body with areas of normal skin in between

(Figure 11). The patient came to the outpatient department the next day after receiving the vaccine and was treated with tablet cetirizine 10mg twice daily for 7 days along with calamine lotion. On follow up after 7 days patient gave history of resolution of lesions within 1-2 days of initiating treatment. The patient was contacted telephonically to enquire if he took the 2nd dose of the vaccine, which he denied due to the fear of developing similar lesions again.



Figure 11: Wheals present all over body with areas of normal skin in between

Patient 6 was a 26 year old male who presented with complaints of intensely pruritic rash primarily over the face, upper limbs and lower limbs 12 hours after 1st dose of COVISHIELD™ vaccine. There was no history suggestive of angioedema, difficulty in breathing, any systemic symptoms, skin disease, reactions after other vaccinations or medications or similar lesions due to any triggers. On examination, there were erythematous, urticarial wheals all over the face, upper limbs and lower limbs. The patient presented to the outpatient department the next day after receiving the vaccine and

was managed with tab cetirizine 10mg twice daily for 7 days along with calamine lotion. On follow up after 7 days patient gave history of resolution of lesions within 4-6 hours of initiating treatment. The patient gave history of taking the 2nd dose of the vaccine; however he did so while initiating therapy with antihistamines prior to vaccination and continued same treatment for 15 days after vaccination and did not develop urticarial rash after the 2nd dose.

A summary of the various mucocutaneous adverse effects observed at our institute is mentioned in Table 1.

Table 1: Summary of the various mucocutaneous adverse effects post COVISHIELD™ vaccine

S. No.	Case	Age	Sex	Dose 1	Dose 2
1	Photoallergic Dermatitis	40yr	Male	1-2days after 1 st dose	2 nd dose not taken
2	Herpes Simplex Reactivation	32yr	Female	1 day after 1 st dose	Patient lost to follow up
3	Pompholyx	32yr	Male	No reaction with 1 st dose	Pompholyx: 2 days after 2 nd dose of vaccine
4	Urticaria	25yr	Male	1 hour after 1 st dose	No history of similar lesions with 2 nd dose
5	Urticaria	28yr	Male	6hours after 1 st dose	2 nd dose not taken
6	Urticaria	26yr	Male	12hours after 1 st dose	2 nd dose taken with antihistamine therapy 15 days prior and after vaccination, no history of urticarial lesions.

Discussion

Vaccination has played an essential role in the advancement of global health. Some of the world's deadliest diseases like smallpox have been eradicated with the help of vaccines and many others have been controlled. The sudden emergence of the COVID 19 pandemic and its impact on global health meant that the development of effective and safe vaccines was crucial for this new lethal disease. So far, there are three main types of COVID-19 vaccines in use

around the world: mRNA-based vaccines, adenoviral vector vaccines, and inactivated whole-virus vaccines [5].

Since the introduction of vaccines for the COVID-19 disease, various reports of a spectrum of mucocutaneous side effects have surfaced [6-8]. Often these reactions are mild to moderate in nature, however in rare instances severe reactions like anaphylaxis have been reported [9].

Presently, the common types of COVID-19 vaccines widely being used across the world are Messenger ribonucleic acid (mRNA) vaccines like BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna), Adenoviral vector vaccines including ChA-dOx1 nCoV-19 (AstraZeneca) and Ad26.COV2.S (Johnson and Johnson's) and inactivated whole-virus vaccines such as BBIBP-CorV (Sinopharm) and CoronaVac (Sinovac) [10]. COVISHIELD™ manufactured by AstraZeneca, is a ChA-dOx1 nCoV-19 type of vaccine. The vaccine contains Polysorbate 80, which is a low-molecular weight molecule (hapten) with a polycyclic structure that may act as the photosensitizer.

All of the vaccine reactions observed in our case series, occurred due to the COVISHIELD™ vaccine as that was the vaccine being administered at our institution and it is noteworthy that all the reactions resolved on treatment for short duration. None of the patients gave history of any dermatological conditions prior to the onset of reaction due to vaccination. This finding is consistent with study conducted by McMahon *et al* [11] which reported that 84% of vaccination reactions occurred in individuals with no previous dermatologic history.

Farinazzo *et al* [12] postulated that the urticarial wheals may be associated with polyethylene glycol-2000 (PEG-2000) present in the vaccines. However, the vaccine in our study (COVISHIELD™) does not have PEG-2000. The urticarial rash may be associated to the inactive constituents of the vaccine and warrants further research [6]. An interesting observation noted in our case series was the incidence of photoallergic dermatitis, which may be attributed to Polysorbate 80, a polycyclic hapten that acted as the photosensitizer. Other types of reactions that have been reported with the COVISHIELD™ vaccine include injection

site reactions (pain, erythema, burning sensation, swelling), morbilliform rash, pityriasis rosea like eruption, purpura, erythema multiforme, aphthous ulcers and telogen effluvium [6]. Herpes simplex virus reactivation and urticaria are adverse reactions that have been described in earlier reports [13,14]. However, our findings suggest pompholyx and photoallergic dermatitis as novel adverse reactions to the COVISHIELD™ vaccine.

With the aid of this case series we would like to highlight the different types of cutaneous adverse effects that can be observed post vaccination with the COVISHIELD™ vaccine. It is important to note that while a variety of adverse reactions can occur due to the vaccine, it should not be a contraindication or discourage vaccination for the general population. Patients with a history of reaction with the first dose should consult a specialist prior to taking the next dose and report immediately if any mucocutaneous lesions re-appear on taking the next dose.

References

1. Das P, Arora S, Singh GK, *et al*. A study of COVID-19 vaccine (Covishield) induced dermatological adverse effects from India. *Journal of the European Academy of Dermatology and Venereology*. 2022.
2. Kaur U, Ojha B, Pathak BK, *et al*. A prospective observational safety study on ChAdOx1 nCoV-19 corona virus vaccine (recombinant) use in healthcare workers-first results from India. *E Clinical Medicine*. 2021 Aug 1; 38:101038.
3. Watanabe Y, Mendonça L, Allen ER, *et al*. Native-like SARS-CoV-2 spike glycoprotein expressed by ChAdOx1 nCoV-19/AZD1222 vaccine. *ACS central science*. 2021 Apr 2;7(4):594-602.

4. Norris LB, Qureshi ZP, Bookstaver PB, *et al.* Polysorbate 80 hypersensitivity reactions: a renewed call to action. *Community Oncology*. 2010;9(7):425-8.
5. Heinz FX, Stiasny K. Distinguishing features of current COVID-19 vaccines: knowns and unknowns of antigen presentation and modes of action. *npj Vaccines*. 2021 Aug 16;6(1):1-3.
6. Sil A, Jakhar D, Das A, Jagadeesan S, Aradhya SS. Spectrum of mucocutaneous reactions to COVID-19 vaccination: A report from a web-based study from India. *Indian Journal of Dermatology*. 2022 Mar 1;67(2):115.
7. Galván-Casas C, Català A, Muñoz-Santos C. SARS-CoV-2 Vaccines and the skin. *Actas Dermosifiliogr* 2021; 112:828-36
8. Corbeddu M, Diociaiuti A, Vinci MR, *et al.* Transient cutaneous manifestations after administration of Pfizer-BioNTech COVID-19 vaccine: An Italian single-centre case series. *J Eur Acad Dermatol Venereol* 2021;35: e483-5.
9. CDC COVID-19 Response Team; Food and Drug Administration. Allergic reactions including anaphylaxis after receipt of the first dose of moderna COVID-19 vaccine-United States. December 21, 2020-January 10, 2021. *MMWR Morb Mortal Wkly Rep* 2021; 70:125-9
10. García-Montero C, Fraile-Martínez O, Bravo C, *et al.* An Updated Review of SARS-CoV-2 Vaccines and the Importance of Effective Vaccination Programs in Pandemic Times. *Vaccines* 2021, 9, 433.
11. McMahon DE, Amerson E, Rosenbach M, *et al.* Cutaneous reactions reported after Moderna and Pfizer COVID-19 vaccination: A registry-based study of 414 cases. *J Am Acad Dermatol*. 2021;85(1):46-55.
12. Farinazzo E, Ponis G, Zelin E, *et al.* Cutaneous adverse reactions after mRNA COVID-19 vaccine: Early reports from Northeast Italy. *J Eur Acad Dermatol Venereol* 2021;35: e548-51
13. Abidi A, Fatima G, Srivastava S, Chakravorty S. Reports of herpes simplex virus reactivation after COVID vaccination: A case series. *J Intern Med India* 2021; 15:54-5
14. Bawane J, Kataria R, Mohite A, Verma K, Shukla U. Cutaneous adverse effects of the available COVID-19 vaccines in India: A questionnaire-based study. *Journal of the European Academy of Dermatology and Venereology*. 2022 Aug;36(8):e619.