

Adverse cutaneous reactions post Covid-19 vaccination- Case series from a tertiary care centre in Eastern India

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Abstract

Background Since the advent of the novel coronavirus, vaccines have been the most important tool of combat against the raging pandemic. However, several reports of adverse effects following vaccinations including dermatological reactions have emerged.

Methods A descriptive observational study was carried out from June to August 2021 with all patients who presented with a new onset cutaneous reaction within 14 days of vaccination excluding patients with other possible causes of cutaneous reaction, particularly exposure to any drugs.

Results A series of 13 cutaneous reactions post vaccination with the two major vaccines available in India, Covishield and Covaxin have been reported in this series. Most of the reactions were mild and included urticaria, pityriasis rosea, morbilliform rash, whereas some uncommon reactions such as lichen planus and vitiligo were found. Severe reactions were rare, only one case of erythema multiforme major was seen.

Conclusion The pathophysiology of post vaccination cutaneous reaction is still elusive and warrants further research. It is important for the dermatologist to be aware of such adverse events in order to address the common misconceptions and apprehension of people regarding vaccination.

Key words

Covid-19, vaccination, pandemic, adverse cutaneous reaction.

Introduction

The world has plunged into a deep social, economic and health crisis since the advent of COVID-19 pandemic. Over the last three years, as people tend to recover from their personal bereavements, economic and social crisis, governments across the world have ramped up their efforts to develop vaccines and immunize their populations. India too, has developed two vaccines namely, ChAdOx1 nCoV-19 Corona Virus Vaccine (Recombinant)-COVISHIELD,

manufactured by SERUM Institute of INDIA and COVAXIN, India's indigenous COVID-19 vaccine by Bharat Biotech, developed in collaboration with the Indian Council of Medical Research (ICMR) - National Institute of Virology (NIV). Large scale vaccination has already been implemented throughout the country to tide over the waves of the pandemic. Till date, although the clinical manifestations, complications of the disease have gradually unveiled themselves, there is still ample room for research regarding the associations, epiphenomenon, treatment options and prevention of the disease. Amidst the turmoil, the necessity and contribution of the vaccines in order to fight the pandemic is undeniable,

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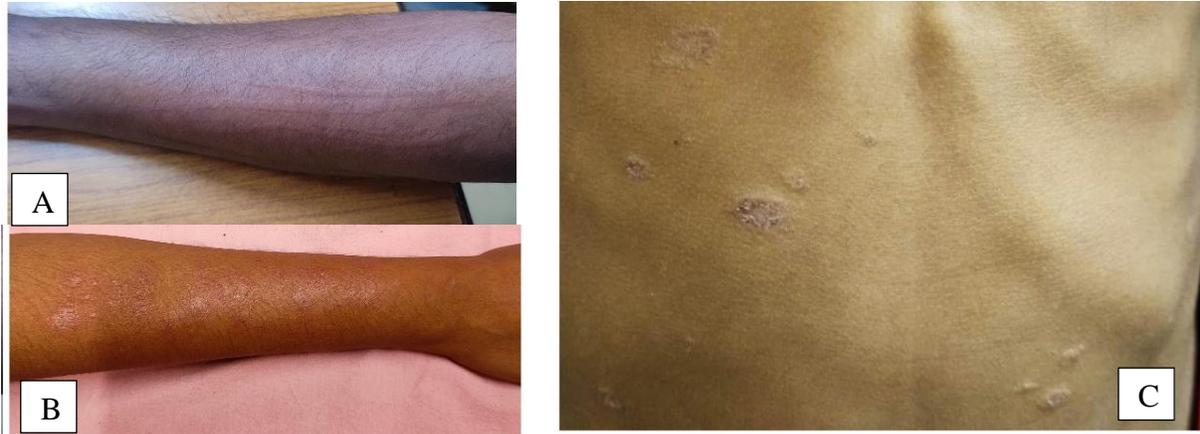


Figure 1 Linear, oedematous, erythematous streaks elicited after scratching- suggestive of dermatographism (A); Multiple, erythematous, maculo-papular eruption over sun exposed areas -extensor surface of hands (B) & neck, suggestive of polymorphic light eruption; Numerous erythematous papulo-squamous lesions (some show collarette scaling) over trunk (C) & upper arms - Pityriasis rosea.

however the impact and long-term effects of vaccination is still shrouded in mystery. Several clusters of cutaneous adverse events related to COVID-19 vaccination around the world has surfaced up in recent literature. There is paucity of data and evidence regarding the same with Indian vaccines. The authors hereby report a series of 13 cases of post-vaccination cutaneous reactions that have been detected in the outpatient department over a period of three months.

Methods

A descriptive observational study was carried out from June to August 2021 after obtaining permission from institutional ethical committee. All patients who presented with a new onset cutaneous reaction within 14 days of vaccination were included and the causality of association ranged from probable to certain. The study excluded patients with other possible causes of cutaneous reaction, particularly exposure to any drugs. After obtaining a detailed history, thorough clinical examination and appropriate diagnostic procedure (if required) a detailed assessment was completed for these patients. The collected data was tabulated and subsequently analyzed followed by comparison

with existing literature. Since adverse reactions following Covid vaccinations are diverse and intriguing, we looked up the literature available on Medline, Pubmed and other databases using MeSH terms like 'Covid 19 vaccine' or 'cutaneous adverse reactions' for information & review.

Results

Out of the 13 cases observed, 8 (61.5%) occurred following second dose of vaccination. 12 (92.3%) cases occurred with Covishield & one (7.7%) case was due to Covaxin. 12 (92.3%) cases were mild and were treated on an OPD basis but one case was diagnosed as Erythema Multiforme Major and required hospitalization. 6 out of 13 patients (46.1%) were males while the rest were females. The mean age of presentation was 32.53 ± 9.85 years. 10 out of 13 cases (76.9%) presented within one week of vaccination. Four cases (40%) presented with systemic symptoms in the form of fever, asthenia, bodyache. Out of 13 cases, 5 (38.46%) were urticaria (2 cases had dermatographism, **Figure 1A**), 2 (15.3%) polymorphic light eruption (PMLE) (**Figure 1B**). One each of pityriasis rosea (**Figure 1C**), erythema multiforme (EM) major (**Figure 2A,B**), eruptive



Figure 2 Multiple target lesions distributed throughout the body (A), haemorrhagic crusts over the lips (B) - Erythema Multiforme Major; multiple, violaceous, polygonal papules- Lichen planus (C).

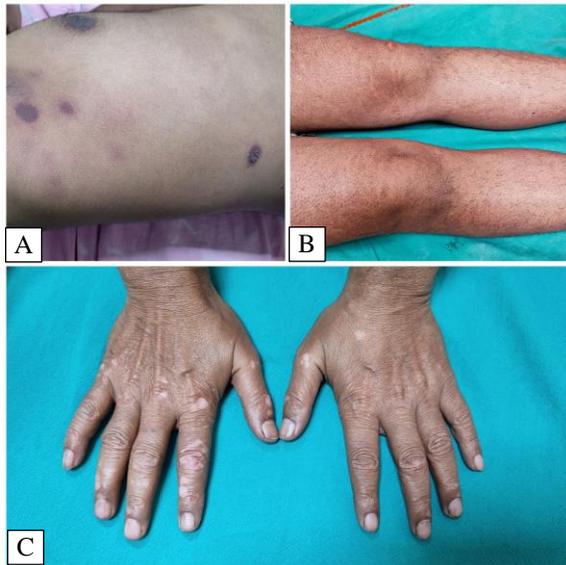


Figure 3 Well circumscribed dusky red patches with overlying bullae in few- generalised fixed drug eruption(A); generalised morbilliform eruption- erythematous macules with confluence (B); Multiple, depigmented macules & patches- vitiligo (C).

lichen planus (**Figure 2C**), generalized fixed drug eruption (FDE) (**Figure 3A**), morbilliform rash (**Figure 3B**), vitiligo (**Figure 3C**) was noted. The distribution of cutaneous reactions

have been illustrated in **Figure 4**. All but one patient (erythema multiforme major) could complete full course of vaccination. The clinical profile of the patients have been tabulated in **Table 1**.

Discussion

The world has been plagued by many infections from time immemorial and vaccines have been the most important weapon of combat against them. The sudden appearance of the Covid 19 infection and its rapid transition into a pandemic necessitated the urgent development of effective vaccines. Three major types of vaccines namely, messenger RNA-based vaccines, adenoviral vector vaccines, and inactivated whole-virus vaccines have been developed globally for prophylaxis against covid infection. Several cutaneous reactions, some immediate & others late are being increasingly reported, the pathomechanisms of which are yet unclear. However, the incidence of such reactions are quite low & the benefit of vaccination outweighs the concerns of such adverse reactions.

According to existing literature, the adverse effects commonly encountered were injection site reactions, urticaria, pityriasis rosea, morbilliform & purpuric rashes, herpes simplex virus/ varicella zoster virus reactivation and thrombotic events.¹ There are reports of facial swelling after dermal filler injection post vaccination as well as flare up or worsening of existing dermatological diseases. The vaccines are essentially derived from the viral genomic sequence. An accelerated immune response against the viral particles or the excipients (inactive substances used for vaccine/ drug delivery that improve solubility, stability or absorption) is the probable mechanism for post vaccination cutaneous reactions. PEG (polyethylene glycol) present in mRNA vaccines and polysorbate 80 found in ChAdOx1 nCoV-19

Table 1 Clinical profile of patients with adverse cutaneous reactions following Covid vaccination; FDE: Fixed drug eruption, EM Major: Erythema multiforme major, PMLE: Polymorphic light eruption.

Sl no.	Age(years)	Gender	Disease type	Vaccine Type	Dose	Clinical presentation
1	19	Male	Generalised FDE	Covishield	Second dose	Fever & cutaneous symptoms within 1 day of vaccination Day after vaccination,
2	44	Female (HIV +)	EM Major	Covishield	First dose	Systemic symptoms + (fever, myalgia, conjunctival congestion)
3	32	Female	Polymorphic light eruption	Covishield	Second dose	A week after vaccination, present since 2 months
4	21	Male	Pityriasis Rosea	Covishield	Second dose	3-4 days after vaccination
5	24	Female	Polymorphic light eruption	Covishield	Second dose	2-3 days post vaccination, persisting for 1 month
6	37	Female	Acute urticaria	Covishield	Second dose	Day after vaccination
7	34	Male	Urticaria (Dermographism)	Covaxin	Second dose	2-3 days post vaccination
8	37	Female	Acute urticaria	Covishield	First dose	Fever, cough,urticaria A wk after vaccination
9	28	Female	Acute urticaria	Covishield	Second dose	A day after vaccination
10	22	Female	Morbiliform rash	Covishield	Second dose	Fever, rash a day after vaccination
11	42	Male	Eruptive lichen planus	Covishield	First dose	Within 2 wks of vaccination
12	52	Male	Vitiligo Vulgaris	Covishield	First dose	Within 4 wks of vaccination
13	31	Male	Urticaria (dermographism)	Covishield	First dose	Within 2 wks of vaccination, gets controlled with antihistamines

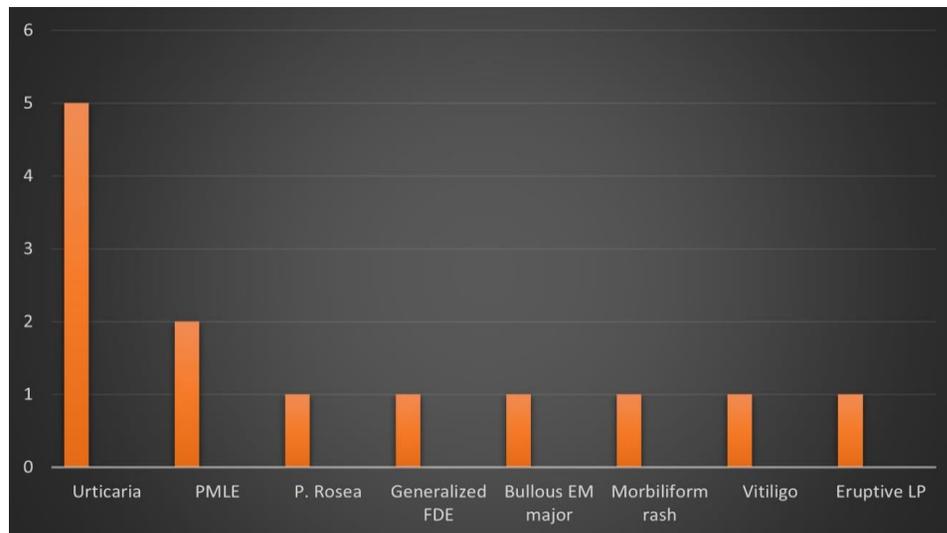


Figure 4 Cutaneous adverse reactions after Covid-19 vaccination: FDE- fixed drug eruption, EM major- erythema multiforme major, PMLE: polymorphic light eruption, LP: lichen planus

(AstraZeneca-Oxford) are two such excipients that have been frequently blamed for inducing allergic reactions.² There are certain reactions like pityriasis rosea, chilblains, erythromelalgia that have been reported after Covid infection as well as vaccination that further supports the fact that the vaccines trigger immune responses similar to that triggered by the virus. The above-mentioned phenomena have been also reported after vaccination against influenza and hepatitis B. Vaccine-specific infectious particles can cause immune dysregulation leading to human herpes virus (HHV-6/7) reactivation and typical pityriasis rosea (PR) eruption or a delayed hypersensitivity response to vaccines can produce a clinical picture similar to medication-induced pityriasis rosea like eruption (PR-LE).³ Merhy *et al.* reported a case of new onset lichen planus after first dose of Pfizer-BionTech vaccination.⁴ There have been previous reports of flare up of lichen planus with this vaccine. In our series, the patient had a past history of lichen planus 10 years back which reappeared two weeks after the first dose of vaccination. Possible activation of Th1 immune response and cytokine release may be the basis for such reaction and it has been previously demonstrated following other infections, drugs and vaccinations.

Another perplexing phenomenon encountered in our series was the development of a new onset vitiligo following second dose of vaccination in a 52-year-old man. Only 3 cases of newly diagnosed vitiligo have been reported post covid vaccination, two with Pfizer and one with Moderna.⁵ Vaccines and viral/bacterial antigens may trigger strong innate immune response reactivating autoimmune diseases. The possible mechanism in this case may be bystander activation and molecular mimicry.

Urticaria, both acute and chronic has been described following Moderna, Pfizer and

Covishield vaccination. A case series by Choi *et al.* describes a case of dermographism in a patient seventeen days after administration of first dose of Pfizer vaccination.⁶ Allergic reaction following vaccination is not infrequent and fortunately it is mostly mild. Rarely life-threatening anaphylaxis may occur. These can be due a reaction to the antigenic component or excipients and may be acute in onset or delayed. Cases of anaphylaxis have been reported after vaccination with mRNA vaccines. Since this is an example of IgE mediated hypersensitivity which requires prior sensitisation, its occurrence following first dose remains unexplained. Allergens that are responsible for IgE mediated reactions are mostly proteins but mRNA vaccines like Pfizer and Moderna do not have proteins. Therefore, complement activation-related pseudoallergy (CARPA) has been postulated as a possible mechanism, but not proven yet.⁷ Polyethylene glycol (PEG) has been found to be offender in some cases. Delayed urticarial reactions corresponds to the beginning of the normal immune/inflammatory response leading to production of cytokines related to non-IgE-mediated mast cell degranulation. Late onset injection site reactions in the form of erythema, pain and swelling that have been seen particularly with Astrazeneca vaccine are considered to be a manifestation of robust humoral and cellular response to the spike protein generated at the injection site by the vaccine.⁷

Fixed drug eruptions are a type of adverse drug reactions characterised by recurrent, identical skin eruptions that tend to involve the same anatomical sites after exposure and re-exposure of the offending agent. It is a type of delayed hypersensitivity reaction mediated by CD8+ T cells with an average latency period of 0-40 days.⁸ Three case reports of bullous fixed drug eruptions have been reported so far- two cases with the mRNA vaccine (Moderna) and one with

the viral vector vaccine (Oxford-AstraZeneca, ChAdOx1).⁹ In our case, the patient had no history of prior self-medication and the lesions developed a day after the second dose of vaccination. The patient presented with fever and multiple, dusky red patches and few bullous lesions all over the body including genitalia which responded well to a short course of oral methylprednisolone healing with residual hyperpigmentation.

Erythema multiforme (EM) is another immune mediated muco-cutaneous adverse reaction that has been reported following vaccination. Depending upon the severity and type of involvement it can be EM major or EM minor and can be often clinically diagnosed. Few cases of EM have been reported after Pfizer, Moderna and CoronaVac vaccines. Vaccine antigens may induce T helper type 1 mediated cellular inflammation.¹⁰ The latency period is usually within 2 weeks of vaccination. In our case, a 44-year-old HIV patient presented with fever, malaise and generalised, target-like, pruritic lesions within one day of receiving first dose of vaccination. The lesions first appeared on the lips and gradually progressed to involve the arms, legs and trunk in that order and developed central bullae. The total involvement was <10% of body surface area (BSA). There was no history of any recent infection or intake of new drugs (except antiretroviral therapy). Based on clinical features, patient was diagnosed as a case of erythema multiforme major and was

immediately hospitalised to be treated with short course systemic steroids and supportive care. Patient was discharged but lost on follow up.

There have been reports of generalised pruritic morbilliform rashes after Covid vaccination. Das *et al.* reports 4 cases of maculopapular rash post-vaccination.¹¹ Ohsawa *et al.* has reported a case of morbilliform eruption mimicking natural covid infection after Pfizer mRNA vaccine.¹² Immune response to vaccine (containing viral genome) may mimic that of natural infection and produce similar cutaneous as well as systemic symptoms. In our case, a 22-year-old female developed fever, asthenia and generalised morbilliform, pruritic, blanchable rash a day after second dose of vaccination. A thorough evaluation negated a possible infective etiology. Based on temporal association, the rash was attributed it to the vaccination. She was given symptomatic management with anti-pyretics, antihistamines and emollients. Recovery was uneventful. Agarwal *et al.* reported a series of 16 cases with Covishield and Covaxin.¹³ A brief comparison between our study and Agarwal *et al.* has been tabulated in **Table 2**.

Some of the reported adverse events may be purely coincidental and further research can only prove and establish a causal relationship between vaccine and these cutaneous reactions. However, dermatologists must be vigilant enough so that they are better equipped to inform, counsel and reassure patients.

Table 2 Comparison between our study and study by Agarwal *et al.*[13]

		<i>Our study</i>	<i>Agarwal et al.</i>
No. of cases due to	Covishield	12	4
	Covaxin	1	12
No. of cases after	1 st dose	5	7
	2 nd dose	8	9
Types of reactions		Urticaria(majority), Pityriasis Rosea, generalised pruritus, Injection site reaction, Herpes Zoster etc.	Urticaria (majority), Pityriasis Rosea, Fixed drug eruption, PMLE, EM Major, Lichen planus, Vitiligo, Morbilliform rash

Conclusion

Vaccine induced skin reactions are usually rare and mostly harmless. However, the authors strongly encourage vaccination to fight the pandemic that has turned our world upside down. Increasing reports may add to literature regarding possible cutaneous reactions post-vaccination, although causal relationship remains to be established. The outcome of patients in this series was good and all patients completed their vaccination barring one. A compact knowledge on these cutaneous reactions may aid the dermatologist to address the fear and misconceptions that may hinder vaccination.

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