

Lichenoid Drug Eruption Following COVID-19 Vaccination: A Series of Four Cases

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Abstract

Since the beginning of the coronavirus disease (COVID-19) pandemic, several cutaneous manifestations following COVID-19 vaccination have been reported, most commonly local injection site reactions. However, lichenoid drug eruptions are rarely seen. There is scant information about its occurrence following the vaccine, especially the COVID-19 vaccine. To the best of our knowledge, there have been only three case reports regarding the development of lichenoid drug eruption after receiving the COVID-19 vaccine. Herein, we report the first case series of lichenoid drug eruption induced by COVID-19 vaccine, which has been proved by history taking, clinical findings, and histopathology.

Keywords: *Lichenoid drug eruption; Vaccination; COVID-19 vaccine; SARS-CoV-2*

1. Introduction

Due to the increasing incidence of coronavirus disease worldwide, many dermatologic reactions have been reported with mass vaccination against SARS-CoV-2 [1]. Lichenoid drug eruption is a rare cutaneous adverse effect associated with several drugs; it uncommonly occurs after vaccination [2-4]. Although infrequent, there are some reports of lichenoid eruptions as a cutaneous manifestation of COVID-19 vaccination [5-7]. To the best of our knowledge, we report the first case series of lichenoid drug eruptions secondary to COVID-19 vaccine, which has been proved by history taking, clinical examination, and histopathology.

2. Case Descriptions

We describe four patients who developed lichenoid drug eruptions (LDE) after the COVID-19 vaccine.

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2.1 Case 1

A 67-year-old male with a history of penicillin allergy, presented to our department for a 2-month history of a disseminated pruritic eruption. Lesions had appeared 3 days after the second dose of the Oxford-AstraZeneca COVID-19 vaccine. Physical examination showed multiples erythematous and violaceous scaly papules and plaques on the thigh, neck, upper chest area and forearms (FIG.1). He did not show any oral, ungueal, or scalp involvement. He denied any drug ingestion or chemical exposure. Laboratory investigation results were unremarkable. Two biopsy specimens came from generalized eruptions showed a consistent with a lichenoid drug reaction. The epidermis had focal parakeratosis, containing a micro cyst and a pustule under the cornea, necrotic keratinocytes and comprising an eosinophilic polynuclear exocytosis (FIG.1). Degressive topical corticotherapy was prescribed with an improvement of the symptomatology.



FIG. 1. a, b: Confluent violaceous and infiltrate papules and plaques located on thighs and upper chest area, c: Biopsy specimen showing acanthosis of the epidermis, focal parakeratosis. The superficial dermis is edematous, with a polymorphic lichenoid and perivascular inflammatory infiltrate made of lymphocytes, eosinophilic polynuclears and some neutrophilic polynuclears with numerous necrotic keratinocytes (HE. $\times 40$)

2.2 Case 2

Patient 2 was a 20-year-old woman, presented at 37 weeks gestation, who has taken antituberculosis drugs for 5 months. She developed multiple violaceous papules approximately one day following her first dose of Sinopharm COVID-19 vaccine. It started on the arms and then spread progressively throughout the entire body, including the face. She had no prior dermatological issues or other skin diseases. There was no recent infection and no recent change in her usual treatment. Physical examination showed disseminated violaceous, shiny, flat, confluent polygonal papules and plaques all over the body, with confluence on the abdomen (FIG. 2). A skin biopsy was performed, showing irregular epidermal hyperplasia and a moderately dense lichenoid lymphocytic infiltrate, with the presence of apoptotic keratinocytes and scarce eosinophils in the dermis (FIG. 3). The eruption started to heal after treatment with topical clobetasol propionate, even though the patient continued to take anti-tubercular drugs.



FIG. 2. Disseminated violaceous, brownish, shiny, flat, confluent papules and plaques all over the body.

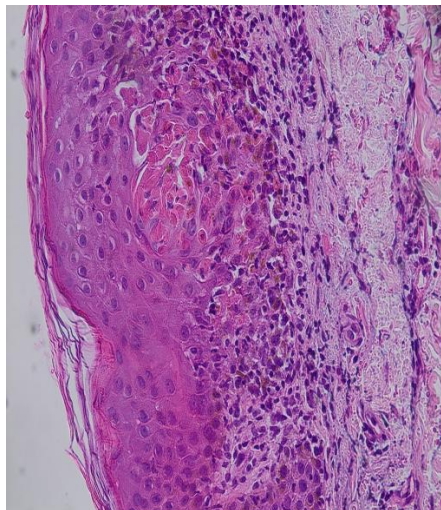


FIG. 3. The superficial dermis is the site of a dense lympho-histioid infiltrate with eosinophilic polynuclears associated with a discrete pigmentary incontinence and a focal necrotic keratinocytes Hematoxylin-eosin stain*40.

2.3 Case 3

A 28-year-old male with no significant past medical history, presented to our department with a 12-week history of intense pruritic eruption, which occurred 15 days after receiving the second dose of Sinopharm COVID-19 vaccine. He denied any history of infection in the previous months.

Dermatological examination revealed numerous, violaceous, coalescing papules over the limbs, thighs, and arms (FIG. 4). The mucosae as well as the hair and nails, were uninvolved. The clinical diagnosis of lichenoid drug eruption was confirmed by

histology, which revealed focal lichenoid dermatitis with necrotic keratinocytes and a minimal eosinophilic component (FIG. 4). Routine blood tests were within normal ranges. Moreover, HCV and HBV serological markers were negative. The patient showed some improvement with topical Clobetasol propionate and antihistamines.

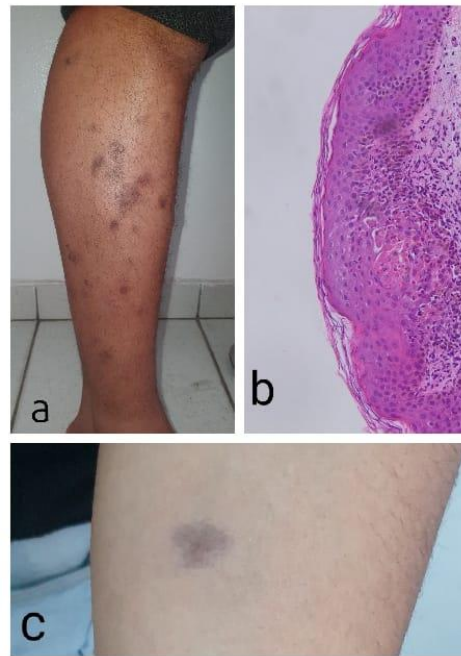


FIG. 4. a, c: Violet-colored, flat-topped papules and plaques on lower legs and left arm, b: Image of LDE: The epidermis is focally acanthotic, orthokeratotic, with focal parakeratosis, discrete focal spongiosis and lymphocytic exocytosis with inflammatory cells penetrating the epidermal basal layer, with necrotic keratinocytes and a minimal eosinophilic component (HE. $\times 20$).

2.4 Case 4

A 65-year-old female patient was referred to our department due to a disseminated erythematous and itchy eruption. Her past medical history revealed hypertension, asthma, and her daily medications (without any recent adaptations) included IC, ARAII, Levothyrox, Seretide, and Ventolin. She had no previous history of any dermatological disease. Regarding COVID-19 vaccination, the patient received her first and second dose of AstraZenca vaccine without any complications. Thirty days after the third dose of Sinopharm vaccine (administered 1 year after the second shot), she noticed several pruritic, polygonal, purple papules appeared on the patient's thighs, which quickly spread with time extending to the whole body. Physical examination revealed violaceous planar papules and plaques on the chest, lumbar back, extensor, flexural extremities, dorsal hands, palms, and soles (FIG. 5). Mucous membranes and nails appeared normal. A skin biopsy was performed, showing focal parakeratosis, irregular epidermal hyperplasia, and a moderately dense lichenoid lymphocytic infiltrate with necrotic keratinocytes and scattered eosinophils in the dermis. The patient's cutaneous symptoms showed some improvement with antihistamines and topical corticosteroids.

Patient demographics, as well as vaccination history, clinical presentation, and histopathologic features are summarized in TABLE 1.



FIG. 5. Polygonal, shiny, purple, papules all over the body.

TABLE 1. Patient demographics, medical history, clinical presentation, and histopathologic features.

Patients	Sex	Age	Vaccine	Dose	Onset to rash	Distribution of the lesions	Histopathological features
Patient 1	M	67	Astrazeneca	Second	3 days	Thigh, neck, upper chest area and the forearms	focal parakeratosis, keratinocyte necrosis eosinophilic polynuclear exocytosis
Patient 2	F	20	Sinopharm	First	2 months	Entire body	epidermal hyperplasia dense lichenoid lymphocytic infiltrate apoptotic keratinocytes eosinophils in the dermis
Patient 3	M	28	Sinopharm	Second	15 days	Limbs, thighs, and arms	necrotic keratinocytes minimal eosinophilic component lymphocytic exocytosis
Patient 4	F	65	Sinopharm	Third	1 day	Entire body	focal parakeratosis, irregular epidermal hyperplasia, dense lichenoid lymphocytic infiltrate Necrotic keratinocytes scattered eosinophils in the dermis.

3. Discussion

Lichenoid drug eruption is a rare side effect that can occur following the administration of several different medications. However, there is scant information about its occurrence following vaccine especially COVID-19 vaccine [1]. In a registry-based study of 414 patients with cutaneous reactions following COVID-19 mRNA vaccines, only one patient experienced lichenoid drug eruption, which seems to be very rare [1]. Recently, to the best of our knowledge, at the time of this report, there has been only three reports in the literature of LDE following the administration of different types of COVID-19 vaccine [5-7]. However, lichenoid drug eruption due to non-mRNA COVID-19 vaccines is poorly reported.

The course of LDE related to vaccination was shorter than that observed in lichenoid eruption associated with other drugs. In our study, the median time to onset of vaccine-related LDE was 12 days, consistent with a case series by Yi Chun Lai et al and Sato et al suggesting that such adverse reactions mainly occurred within 2 weeks after vaccination [8,9]. That was also consistent with LDE following COVID-19 Vaccine [5,7].

Among patients who received COVID-19 vaccines, LDE has been reported following the first dose in one patient and second dose in two patients; no case of eruption resurgence was described with the third dose because no reintroduction was performed. Our patient has received a different type of vaccine on the third dose.

The pathogenesis of LDE still is not fully understood. Similarly, to influenza and hepatitis B vaccines, it may be caused by both dysregulation of immune system due to viral components and vaccine adjuvants. IT is thought that CD8+ T cytotoxic cells formed against basal keratinocytes play an important role [10-13]. The mechanisms responsible are yet to be understood.

LDE may appear identical to lichen planus (LP) clinically and histologically. The distribution pattern of LDE may be more generalized than classic LP. Furthermore, these lesions typically spare the classic sites of lichen planus, such as the flexor surfaces, nails, mucous membranes, and genitalia, and often do not exhibit Wickham's striae [11,12]. None of our patients had any hair, oral, genital or nail involvement as in the literature.

Regarding histopathology, several findings are more typical of LDE: focal parakeratosis with interruption of the granular layer, keratinocyte necrosis, as well as eosinophils within inflammatory cells [5,13]. We have obtained similar results in our study. On histopathological examination, three of our cases showed a focal parakeratosis, Eosinophils, and Keratinocytes necrosis were a prominent feature in all our cases.

As for criteria of intrinsic and extrinsic imputability; In this case reports, intrinsic imputability is plausible, but extrinsic imputability is undefined due to the lack of scientific publications for COVID-19 vaccines.

Regarding treatment, topical corticosteroids are the first-line treatment for LDE. In patients who have contraindications to corticosteroids or fail corticosteroids, acitretin may be considered as a potential second-line therapy [6]. In all our cases, local corticosteroids showed a rapid response.

4. Conclusion

This report highlights a rare and clinically significant dermatologic side effect of COVID-19 vaccine. The clinical findings, the short time intervals between vaccination and the appearance of the skin eruption, and the histopathologic findings were consistent with a lichenoid drug eruption following COVID-19 vaccine. Although, given the benefits of the vaccine in the current pandemic, such rare reactions should not discourage vaccination against a life-threatening virus.

REFERENCES

1. McMahon DE, Kovarik CL, Damsky W, et al. Clinical and pathologic correlation of cutaneous COVID-19 vaccine reactions including V-REPP: a registry-based study. *J Am Acad Dermatol.* 2022;86(1):113-21.
2. Asarch A, Gottlieb AB, Lee J, et al. Lichen planus-like eruptions: an emerging side effect of tumor necrosis factor-alpha antagonists. *J Am Acad Dermatol.* 2009;61(1):104-11
3. Tarakji B, Ashok N, Alakeel R, et al. Hepatitis B vaccination and associated oral manifestations: a non-systemic review of literature and case reports. *Ann Med Health Sci Res.* 2014;4(6):829-36.
4. Lukacs J, Scliemann S, Elsner P. Lichen planus and lichenoid reactions as a systemic disease. *Clin Dermatol.* 2015;33(5):512-9.
5. Merhy R, Sarkis AS, Kaikati J, et al. New-onset cutaneous lichen planus triggered by COVID-19 vaccination. *J Eur Acad Dermatol Venereol.* 2021;35(11):e729-30.
6. Paolino G, Rongioletti F. Palmoplantar lichenoid drug eruption following the administration of Pfizer-BioNTech COVID-19 vaccine., *JAAD Case Rep.* 2022;21:182-4.
7. Ziraldo M, Theate I, Vanhooteghem O. Drug-induced lichenoid exanthema by a vaccine against COVID-19 (Vaxzevria). *Dermatol Rep.* 2021;13(3):9358.
8. Lai YC, Yew YW. Lichen planus and lichenoid drug eruption after vaccination. *Cutis.* 2017;100(6):E6-E20.
9. Sato NA, Kano Y, Shiohara T. Lichen planus occurring after influenza vaccination: report of three cases and review of the literature. *Dermatology.* 2010;221(4):296-9.
10. Yawalkar N, Pichler WJ. Mechanisms of cutaneous drug reactions (in German). *J Dtsch Dermatol Ges.* 2004;2:1013-23.
11. Sidikov A, Zaslavsky D, Sadykov A, et al. The new differential diagnostic test for the lichenoid drug eruption. *Dermatol Ther.* 2020;33(6):e13784.
12. Antiga E, Melani L, Cardinali C, et al. A case of lichenoid drug eruption associated with sildenafil citratus. *J Dermatol.* 2005;32(12):972-5.
13. Van den Haute V, Antoine JL, Lachapelle JM. Histopathological discriminant criteria between lichenoid drug eruptions and idiopathic lichen planus: retrospective study on selected samples. *Dermatologica* 1989;179(1):10-3.