Xu *et al. Virology Journal* (2025) 22:57
https://doi.org/10.1186/s12985-025-02653-6

Virology Journal

CASE REPORT Open Access

Unique skin nodules following COVID-19 vaccination: a case report of cutaneous plasmacytosis and review of the literature

Xiaoxi Xu[1*†], Wuwu Ding[2†], Haizhen Song[1] and Dong Wang[1]

Abstract

Background Cutaneous plasmacytosis (CP) is a rare disorder that may affect two or more organ systems, such as skin, lymph nodes or lungs. The pathogenesis of CP remains unknown, and in most cases, the condition follows a chronic and benign clinical course without spontaneous remission.

Case presentation A 50-year-old male who developed necrotizing skin nodules without other systemic abnormalities four days after the first doses of the Coronavirus disease 2019 (COVID-19) vaccination. Oral prednisone improved the lesions by approximately 70%. However, signs of CP recurrence manifested 15 days after the second dose of COVID-19 vaccination. Ultimately, the patient experienced spontaneous remission after contracting SARS-CoV-2 infection.

Conclusion This case uniquely associates COVID-19 inactivated vaccine with CP, where the same lesions appeared after two vaccinations and subsequently resolved following SARS-CoV-2 infection. This provides valuable clinical data for future studies on viral infections and cutaneous B-cell immunity.

Keywords Cutaneous plasmacytosis, COVID-19 vaccine, Skin adverse reactions, IL-6, Cutaneous immunity, Immune tolerance

Background

Cutaneous plasmacytosis (CP), first reported in 1976, is characterized by red-brown macules, papules and plaques with histopathology revealing a dermal infiltration of mature plasma cells [1]. Polyclonal hypergammaglobulinemia is a common symptom observed in 88–93% cases [2]. The condition was originally labeled "cutaneous plasmacytosis" but later renamed "cutaneous and systemic plasmacytosis" to reflect lymphoplasmacytic infiltration beyond the skin [3]. COVID-19 is a multisystem disease affecting several vital organs and has been a global pandemic from 2020 to 2023 [4]. The phenomenon of reactive plasmacytosis was observed in lung and bone marrow tissues of both fatal and non-critical COVID-19 pneumonia patients [5, 6]. Moreover, a 55-year-old woman developed cutaneous Rosai-Dorfman-Destombes disease with polyclonal plasmacytosis three months after being infected with COVID-19 [7]. Here, we describe a case of a patient who developed diffuse skin lesions resembling folliculitis following two doses of COVID-19 vaccines. Histopathological examination showed numerous mature plasma cell infiltrating with significant

†Xiaoxi Xu and Wuwu Ding have contributed equally to this work.

*Correspondence:
Xiaoxi Xu
410127242@qq.com
[1]Department of Dermatovenereology, Deyang People's Hospital, NO.173, Taishan North Road, Jingyang District, Deyang, Sichuan 618000, China
[2]Department of Pathology, Deyang People's Hospital, Deyang, China

neutrophil presence. This case highlights a unique trigger, clinical manifestation and outcome of CP.

Case presentation

A 50-year-old male developed multiple oval-shaped, red papules and nodules (0.5–3 cm in diameter) on his trunk four days after receiving the first dose of the COVID-19 vaccine (CoronaVac, a inactivated vaccine, inoculation date: February 22, 2021). Despite the lesions, he reported no pain or itching. There were no preceding symptoms such as fever, cough, pharyngalgia, or muscle aches documented within one week prior to the onset of the condition. Initially, he was diagnosed as "folliculitis" and "insect bite dermatitis" in local hospital. Systemic treatment with amoxicillin and doxycycline were ineffective. Upon seeking treatment at our clinic, some of the lesions exhibited signs of necrosis and ulceration (Fig. 1). Polarized-light dermoscopy revealed violet lesions with yellow unstructured area in the center, as well as dotted and linear blood vessels, accompanied by white stripes. Most of these vessels and stripes were distributed radially around the center (Fig. 2).

The patient appeared in good spirits, with normal body temperature, respiratory rate, and heart rate. Physical examinations of the chest and abdomen revealed no abnormalities, and there was no enlargement of the superficial lymph nodes throughout the body. A skin biopsy revealed a significant infiltration of mature plasma cells throughout the dermis, along with a central necrosis area characterized by lymphocyte and neutrophil infiltration (Fig. 3). In addition, the results of immunohistochemical analysis of plasmacytoid cells in the superficial dermis showed that CD20 and CD5 were negative, CD79a, CD138, and CD38 were positive, and the MIBI-1 proliferation index was low. Lymphocyte clonality analysis did not find monoclonal gene rearrangement of IgH, IgK, and TCRG. On laboratory evaluation, complete blood cell count, as well as liver and kidney functions, were within normal parameters. Serologic tests for HIV and syphilis yielded negative results. Additionally, serum protein electrophoresis, serum immunofixation electrophoresis, and free light chain levels in urine were all within the normal range.

The patient was diagnosed with CP. After a two-week treatment of oral prednisone 30 mg/d, the lesions improved by approximately 70%. Subsequently, the patient continued to receive the second dose of COVID-19 vaccine (inoculation date: March 24, 2021). Fifteen days later, signs of CP recurrence manifested on the patient's skin. Despite this recurrence, the patient did not seek for medical help, resulting in no improvement in his skin condition for two years. In November 2023, the patient developed symptoms of fever, muscle soreness, hoarse voice and coughs with a throat swab test confirmed a positive result for SARS-CoV2. After taking three doses of ibuprofen sustained-release capsules (300 mg) and one dose of acetaminophen tablets (500 mg), those symptoms relieved. By December 2023,

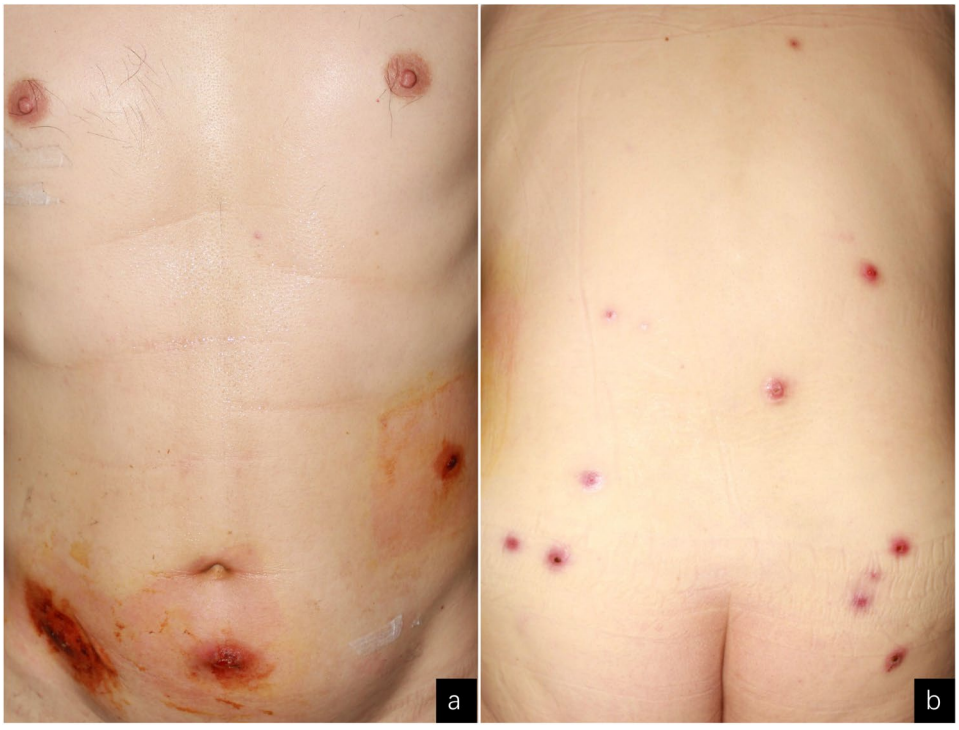

Fig. 1 Multiple red papules and nodules appeared on the trunk of the patient after injection of the COVID-19 vaccine, and some nodules were necrotic

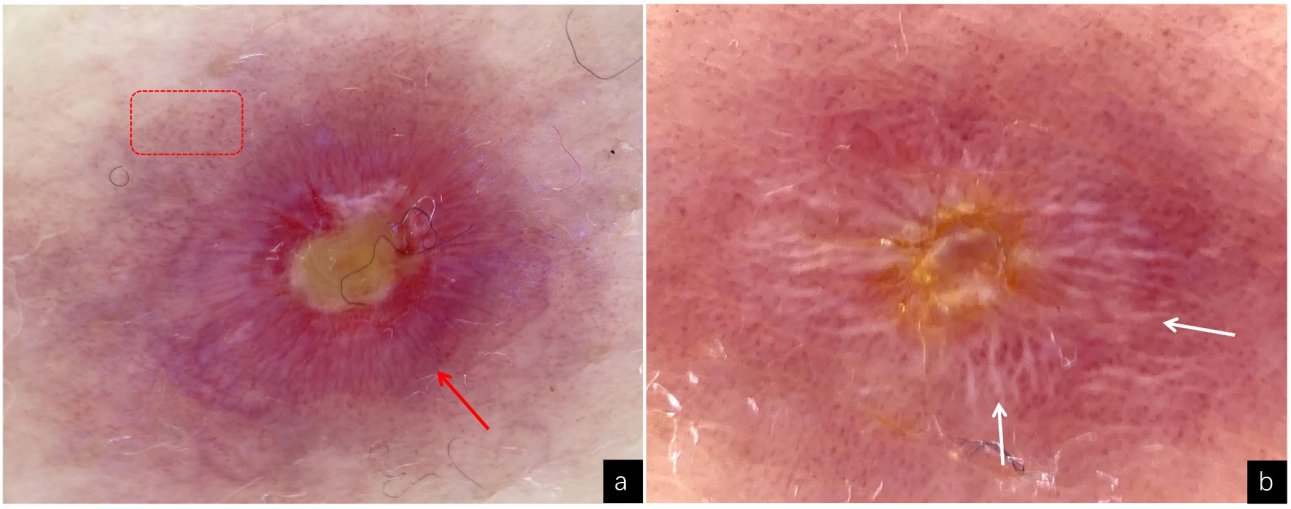

Fig. 2 (**a**) Polarizing dermoscopy showed a yellow unstructured area in the center of the violet lesion, with radial lines (red arrows), and punctiform (red box) vessels around the center (×50). (**b**) White stripes were radial arranged (white arrows)(×50)

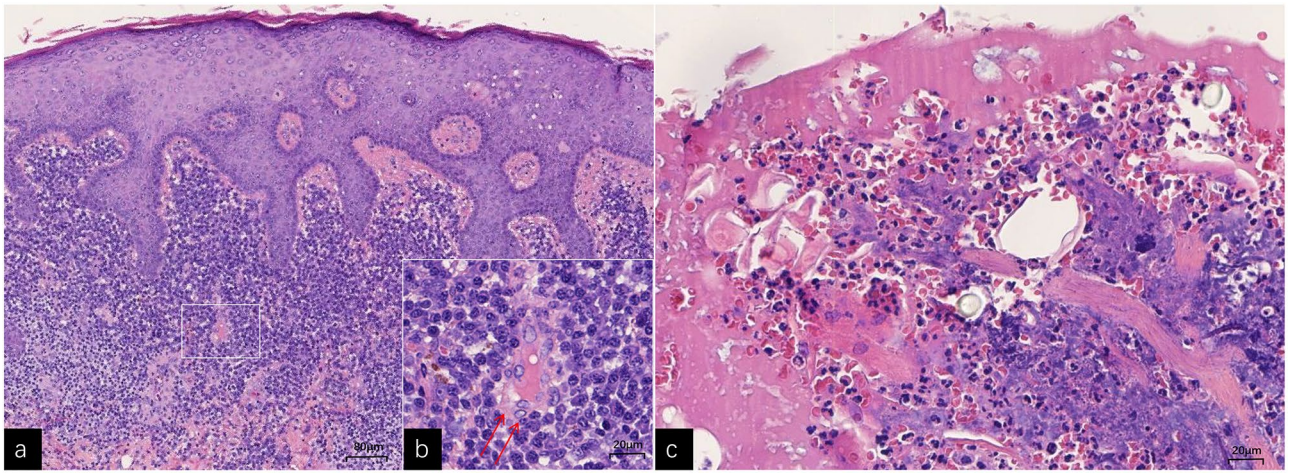

Fig. 3 (**a**) Biopsy showed extensive plasma cell infiltration (**a**) across the dermis, with capillary lumen occlusion (white box). (**b**) The magnified view of the white box area in (**a**). (**c**) Epidermal and dermal necrosis with neutrophil infiltration can be observed in the center of the lesion

the patient's skin lesions began to subside spontaneously, demonstrating no recurrence to date. The patient has been followed up for nearly four years since the onset skin lesions, no abnormalities in other organ systems have been observed (Fig. 4).

Discussion and conclusions

Common local reactions to vaccines include pain, swelling, and redness at the injection site. Systemic reactions include fever, irritability, drowsiness, and rashes [8]. A review was conducted on PubMed using the following search terms: COVID-19 inactivated vaccine, dermatology, rash, skin, cutaneous, CoronaVac, Sinopharm, and Covaxin. The search covered the period from March 1, 2020, to November 30, 2024. A total of 1,091 cases of vaccine-related skin adverse reactions (excluding injection site reactions) were identified. These included type I hypersensitivity reactions, such as urticaria (341, 31.26%) and angioedema (128, 11.73%). Type II hypersensitivity reactions included purpuric rashes and vasculitis (24, 2.20%). Type IV hypersensitivity reactions encompassed morbilliform eruption (387, 35.47%), erythema multiforme (3, 0.27%), and toxic epidermal necrolysis drug eruption (TEN) (2, 0.18%). Additionally, autoimmune-mediated reactions were reported, including lichen planus (9, 0.82%), bullous pemphigus (4, 0.37%), pemphigus (3, 0.27%), vitiligo (1, 0.09%), and alopecia areata (2, 0.18%). Cases of pityriasis rosea, scleromyxedema, pyoderma gangrenosum, chilblain-like lesions, and herpes zoster have also been documented (Table 1) [9–20]. Plasmacytosis has been sporadically reported following injections of other vaccines. Steve et al. [21]. observed atypical lymphocyte infiltration at the injection site in two patients who received the influenza vaccine. One

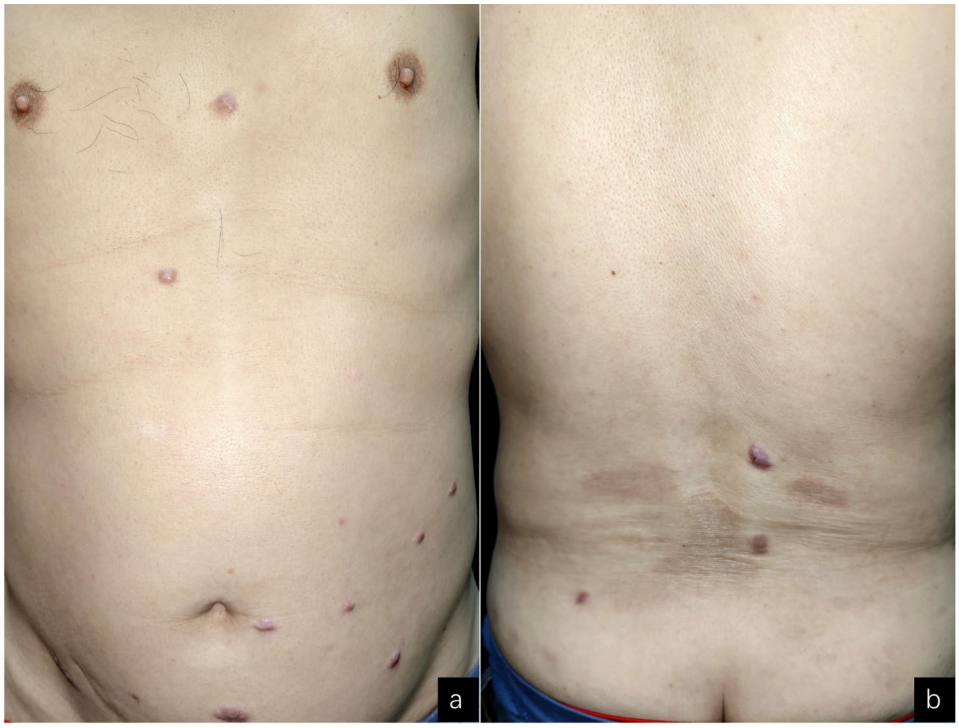

Fig. 4 The clinical pictures from the latest follow-up showed that the patient currently does not have any CP lesions on his body, and part of the old lesions have transformed into scar tissue

Table 1 Cutaneous adverse reactions related to inactivated COVID-19 vaccines

Cutaneous adverse	Case number and proportion			
	CoronaVac	Sinopharm	Covaxin	Total
Urticaria	118(37.46%)	212(28.49%)	11(35.48%)	341(31.26%)
Angiodema	19(6.03%)	109(14.65%)	0(0)	128(11.73%)
Herpes Zoster	5(1.59%)	5(0.67%)	2(6.45%)	12(1.10%)
Morbilliform	8(2.54%)	376(50.54%)	3(9.68%)	387(35.47%)
Pityriasis rosea	29(9.24%)	6(0.81%)	5(16.13%)	40(3.67%)
Rash/Unspecified cutaneous eruption	118(37.46%)	8(1.08%)	0(0)	126(11.55%)
Chilblains-like/Pernio	2(0.63%)	0(0)	5(16.13%)	7(0.64%)
Lichen planus	0(0)	8(1.08%)	1(3.23%)	9(0.82%)
Purpuric rash/Vasculitis	13(4.13%)	7(0.94%)	4(12.90%)	24(2.20%)
Erythema Multiforme	2(0.63%)	1(0.13%)	0(0)	3(0.27%)
Alopecia areata	0(0)	2(0.27%)	0(0)	2(0.18%)
Bullous pemphigoid	0(0)	4(0.40%)	0(0)	4(0.37%)
Pemphigus	0(0)	3(0.40%)	0(0)	3(0.27%)
TEN	0(0)	2(0.27%)	0(0)	2(0.18%)
Vitiligo	1(0.32%)	0(0)	0(0)	1(0.09%)
Scleromyxedema	0(0)	1(0.13%)	0(0)	1(0.09%)
Pyoderma gangrenosum	0(0)	1(0.13%)	0(0)	1(0.09%)
Total case number	315	744	31	1091

patient exhibited perivascular and periadnexal infiltration of lymphoplasmacytic cells with cytological atypia. In the other patient, the skin tissue showed a predominance of multiple types of plasma cells and histiocytic infiltration. Both patients achieved remission following radiotherapy.

The clinical manifestations of folliculitis-like skin papules and nodules in this case posed a challenge in diagnosing CP. Distinguishing features, such as radially arranged blood vessels and white stripes identified through dermoscopy, suggested a differentiation from common folliculitis [22]. Pathological examination in our case revealed epidermal and dermal necrosis with neutrophil infiltration, corresponding to the yellow unstructured area observed during dermoscopy. Fibroplasia and scarring indicated post-necrotic skin repair, aligning with the white stripe structure noted during the examination [23]. Vessels arranged in a radial pattern are commonly found in a variety of tumors, such as keratoacanthoma and squamous cell carcinoma, as well as non-neoplastic diseases like lichen planus, lupus erythematosus, and inverted follicular keratosis [24–26].

The patient did not develop any rashes at the vaccination site, suggesting that the occurrence of CP may not be related to the vaccine adjuvant. Instead, it was the antigens from the carrier that triggered the abnormal immune response. Current evidence indicates that environmental factors, genetic predisposition, or an

infectious etiology may contribute to CP, with a particular emphasis on the dysregulated production of interleukin (IL)-6 in its pathogenesis [2]. IL-6 is the cytokine responsible for B-cell proliferation and terminal differentiation into plasma cells [27]. After vaccine injection, antigen-presenting cells (APCs) phagocytize foreign vaccine antigens, which are processed and presented on their surface by major histocompatibility complex (MHC) class I and II proteins. These APCs then migrate from the antigen-exposed tissue to nearby draining lymph nodes, where they present the MHC complexes to T and B lymphocytes. The activation of T and B cells triggers a response against the antigen, contributing to a potential long-term immune response. Under the influence of helper T cells (CD4 + T cells), B cells rapidly proliferate and form clones. Some of these B cells undergo maturation to become plasma cells, which secrete large amounts of antibodies to combat infection [28]. Normally, the plasma cells were distributed throughout the body through lymphatic vessels and blood vessels, and they migrate specifically to survival "niches" such as bone marrow and lymphatic tissues for long-term retention [29]. A recent study by Gribonika et al., revealed for the first time that the skin can function as an autonomous "tertiary lymphoid organ", by capturing microbial antigens through Langerhans cells, activating functional T cells, promoting B-cell activation, and facilitating the production of specific antibodies by plasma cells [30]. This finding supports previous speculations about the pathogenesis of CP, suggesting that skin tissue may serve as a source of plasmablasts that can mature into fully functional plasma cells. Furthermore, the regulation of IL-6 and other environmental factors enhances the retention and homing abilities of plasma cells in the skin, similar to the presence of other "survival" niches [3], contributing to the cutaneous symptoms of CP.

CP should be differentiated from other conditions resulting in plasma cell proliferation including chronic infection, collagen vascular disease, and generalized cutaneous B-cell pseudolymphoma [31]. Currently, there is no standardized treatment, and patients may be resistant to multiple therapies. Treatments include systemic glucocorticoids, cyclophosphamide, and chemotherapy combined with anti-CD20 antibodies. Thalidomide reduce the progression of CP lesions by reducing IL-6 secretion. While biologics targeting IL-6 could theoretically be applied to CP, there have been no reported cases of successful treatment in patients to date [2, 31]. Most cases of CP follow a chronic and benign clinical course without spontaneous remission [31]. Notably, in this particular case, the skin lesions of the patient gradually diminished following the SARS-CoV2 infection. We speculate that repetitive exposure to the same antigen may have induced immunotolerance, mitigating the aberrant immune response. Regulatory T (Treg) cells and other inhibitory T cells modify the duration, intensity, and chemistry of antigen delivery to immune cells. Additionally, some microbial metabolites in vivo, including short-chain fatty acids like butyric acid, can act on antigen-presenting cells to promote the formation of Treg cells or directly influence the differentiation, migration, and function of pathogenic T cells [32].

In conclusion, this is the first reported case of CP associated with COVID-19 vaccination. Unlike other vaccine-associated skin cases and COVID-19-related skin diseases, this case uniquely associates COVID-19 with CP, where the same lesions appeared after two vaccinations and subsequently resolved following SARS-CoV-2 infection. This provides valuable clinical data for future studies on viral infections and cutaneous B-cell immunity. However, as this is a single case report, confounding variables cannot be excluded during the observation period, and the proposed hypothesis cannot be verified, making it challenging to draw general conclusions. Although uncommon, clinicians should be aware that vaccines have the potential to induce immune disorders in humans. While a benign course is characteristic of CP, patients should be monitored longitudinally for potential disease progression and the possibility of malignant transformation.

Abbreviations

COVID-19	Coronavirus Disease 2019
CP	Cutaneous Plasmacytosis
CD	Cluster of Differentiation
MIBI	Minimally Invasive Biopsy Index
IgH	Immunoglobulin Heavy chain
IgK	Immunoglobulin Kappa light chain
TCRG	T Cell Receptor Gamma Gene
HIV	Human Immunodeficiency Virus
IL	Interleukin
TEN	Toxic Epidermal Necrolysis drug eruption
APCs	Antigen-Presenting Cells
MHC	Major Histocompatibility Complex

Acknowledgements
We would like to thank the patient for granting permission to publish this information.

Author contributions
XX wrote the draft, and critically revised the manuscript and served as the guarantor; WD wrote the draft and revised the manuscript; HS and DW collected data and approved the manuscript. All authors read and approved the final manuscript.

Funding
Science and Technology Project of Sichuan Provincial Health Commission (Award Number: 24WSXT025).

Data availability
All data generated or analyzed during this study are included in this published article.

Declarations

Ethics approval and consent to participate
All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors. Our hospital does not need ethics approval number when publishing a case report. The study obtained written informed consent from the patient.

Consent for publication
Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the signed consent form is available for review by the editor of this journal upon request.

Competing interests
The authors declare no competing interests.

Received: 5 December 2024 / Accepted: 6 February 2025
Published online: 04 March 2025

References

1. Yashiro A, Yashiro E. A kind of plasmacytosis: primary cutaneous plasmacytoma?1976; 86: 910.
2. Wagner G, Rose C, Klapper W, Sachse MM. Cutaneous and systemic plasmocytosis. J Dtsch Dermatol Ges. 2013;11:1161–7.
3. Haque M, Hou JS, Hisamichi K, Tamada K, Cusack CA, Abdelmalek M, et al. Cutaneous and systemic plasmacytosis vs. cutaneous plasmacytic castleman disease: review and speculations about pathogenesis. Clin Lymphoma Myeloma Leuk. 2011;11:453–61.
4. Abebe EC, Dejenie TA, Shiferaw MY, Malik T. The newly emerged COVID-19 disease: a systemic review. Virol J. 2020;17:96.
5. Dorward DA, Russell CD, Um IH, Elshani M, Armstrong SD, Penrice-Randal R, et al. Tissue-specific immunopathology in fatal COVID-19. Am J Respir Crit Care Med. 2021;203:192–201.
6. Rolland-Debord C, Pieroni L, Bejar F, Milon A, Choinier P, Blin E, et al. Cell and cytokine analyses from bronchoalveolar lavage in non-critical COVID-19 pneumonia. Intern Emerg Med. 2023;18:1723–32.
7. Gogia P, Tanni F, Coca-Guzman J, Chen N, Huang Y. Case report: a rare case of Rosai-Dorfman-Destombes disease after the COVID-19 infection. Front Med (Lausanne). 2022;9:1073767.
8. Spencer JP, Trondsen Pawlowski RH, Thomas S. Vaccine adverse events: separating myth from reality. Am Fam Physician. 2017;95:786–94.
9. Avallone G, Quaglino P, Cavallo F, Roccuzzo G, Ribero S, Zalaudek I, et al. SARS-CoV-2 vaccine-related cutaneous manifestations: a systematic review. Int J Dermatol. 2022;61:1187–204.
10. Diab R, Rakhshan A, Salarinejad S, Pourani MR, Ansar P, Abdollahimajd F. Clinicopathological characteristics of cutaneous complications following COVID-19 vaccination: a case series. J Cosmet Dermatol. 2024;23:725–30.
11. Martinez-Ortega JI, Perez-Hernandez F, Fernandez-Reyna I, Eljure Lopez N. First onset of IgA vasculitis and nephritis following COVID-19 vaccination. Cureus. 2023;15:e42448.
12. Corra A, Verdelli A, Mariotti EB, Ruffo di Calabria V, Quintarelli L, Aimo C, et al. Cutaneous vasculitis: lessons from COVID-19 and COVID-19 vaccination. Front Med (Lausanne). 2022;9:1013846.
13. Mohd AB, Mohd OB, Ghannam RA, Al-Thnaibat MH. COVID-19 vaccine: a possible trigger for pyoderma gangrenosum. Cureus. 2022;14:e25295.
14. Parsaei A, Rezaei SS, Rahmani A, Masoumi M, Dehghanbanadaki H, Norouzi S, et al. Scleromyxedema in an adult following Sinopharm BBIBP-CorV vaccination: an extremely rare phenomenon. J Scleroderma Relat Disord. 2023;8:NP9–12.
15. Pourani MR, Shahidi Dadras M, Salari M, Diab R, Namazi N, Abdollahimajd F. Cutaneous adverse events related to COVID-19 vaccines: a cross-sectional questionnaire-based study of 867 patients. Dermatol Ther. 2022;35:e15223.
16. Purushottam M, Rangappa V, Betkerur JB, Kombettu AP, Shastry V. Cutaneous adverse drug reactions (CADRs) to COVID19 vaccines: a case series. Indian Dermatol Online J. 2023;14:383–7.
17. Saraswat N, Tripathy DM, Murali M, Boruah J, Mitra D, Chopra H, et al. A study to describe the pattern of cutaneous adverse effects of COVID-19 vaccines (Covishield and Covaxin). Indian Dermatol Online J. 2023;14:814–20.
18. Shawky A, Elrewiny EM, Gharib K, Sallam M, Mansour M, Rageh MA. A prospective multicenter study on cutaneous reactions reported after Sinopharm COVID-19 vaccination. Int J Dermatol. 2023;62:221–4.
19. 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 J Dermatol. 2022;67:115–20.
20. Tuzer C, Terzioglu K. Evaluation of the autoimmunity and preexisting risky conditions for hypersensitivity reactions to COVID-19 vaccines. Int Arch Allergy Immunol. 2022;183:651–61.
21. May SA, Netto G, Domiati-Saad R, Kasper C. Cutaneous lymphoid hyperplasia and marginal zone B-cell lymphoma following vaccination. J Am Acad Dermatol. 2005;53:512–6.
22. Durdu M, Errichetti E, Eskiocak AH, Ilkit M. High accuracy of recognition of common forms of folliculitis by dermoscopy: an observational study. J Am Acad Dermatol. 2019;81:463–71.
23. Yao QN, Lu YM, Fei WM, Xie CT, Cheng WH, Ren H, et al. Dermoscopy in *Mycobacterium marinum* infection and its correlation with clinical and histopathological features: a prospective observational study. Clin Exp Dermatol. 2023;48:89–95.
24. Fathy H, Ghanim BM, Refat S, Awad A. Dermoscopic criteria of discoid lupus erythematosus: an observational cross-sectional study of 28 patients. Indian J Dermatol Venereol Leprol. 2022;88:360–6.
25. Llambrich A, Zaballos P, Taberner R, Terrasa F, Banuls J, Pizarro A, et al. Dermoscopy of inverted follicular keratosis: study of 12 cases. Clin Exp Dermatol. 2016;41:468–73.
26. Rouai M, Litaiem N, Hammami H, Bacha T, Jones M, Ksontini M, et al. Dermoscopic features of mucosal lichen planus. Int J Dermatol. 2021;60:1368–72.
27. Kaur S, Bansal Y, Kumar R, Bansal G. A panoramic review of IL-6: structure, pathophysiological roles and inhibitors. Bioorg Med Chem. 2020;28:115327.
28. Ding Y, Li Z, Jaklenec A, Hu Q. Vaccine delivery systems toward lymph nodes. Adv Drug Deliv Rev. 2021;179:113914.
29. Tokoyoda K, Hauser AE, Nakayama T, Radbruch A. Organization of immunological memory by bone marrow stroma. Nat Rev Immunol. 2010;10:193–200.
30. Gribonika I, Band VI, Chi L, Perez-Chaparro PJ, Link VM, Ansaldo E et al. Skin autonomous antibody production regulates host-microbiota interactions. Nature. 2024 (Online ahead of print).
31. Leonard AL, Meehan SA, Ramsey D, Brown L, Sen F. Cutaneous and systemic plasmacytosis. J Am Acad Dermatol. 2007;56:S38–40.
32. Bluestone JA, Anderson M. Tolerance in the age of immunotherapy. N Engl J Med. 2020;383:1156–66.

Publisher's note