

Not only toes and fingers: COVID vaccine-induced chilblain-like lesions of the knees

Dear Editor,

During the pandemic caused by SARS-Cov-2 infection, acral chilblain-like lesions (CLL) have been commonly reported cutaneous manifestations of the disease even if their association with the infection has been discussed.^{1,2}

To control the diffusion of SARS-CoV-2 infection, a vaccination campaign is spreading around the world since December 2020; subsequently, several different cutaneous manifestations related to vaccines have been described.³

Here, we describe a 52-year-old woman presenting with purpuric lesions on the knees and lower third of her thighs (Fig. 1a,b). History revealed that the patient underwent the injection of the first dose of ©Moderna mRNA-1273 vaccine on August 2021 and that the lesions had appeared about 7–10 days later. Lesions presented a cold surface and did not show any changes based on temperature. A slight itching sensation and painful walking were referred by the patient, who had never had similar lesions previously in her life. Dermoscopy showed a combination of linear vessels arranged in network fashion with multiple areas of coppery clods, the latter analogously observed in CLL of the toes (Fig. 1c).⁴ Patient was given topical steroids and oral cinnarizine (due to its vasodilator potential) for 2 weeks, and a slow improvement of the lesions was seen with also a fine ending desquamation of the purpuric lesions. Numerous skin

manifestations associated with the virus have been largely discussed, as well as the cutaneous reactions to vaccines.⁵ The latter mostly included pain and swelling on the injection site and localized or diffuse erythematous or urticarial rash, usually associated with an itching sensation. All these lesions were usually transitory with a spontaneous resolution and not associated with systemic symptoms, except for rare cases of angio-oedema and laryngospasm (usually in patients with a well-noted allergic background). Purpuric lesions after vaccination were reported almost exclusively in association with ©Pfizer BNT162b2 mRNA vaccine, and included lesions on the eyelids, systemic purpuric rashes and cases of Henoch–Schonlein purpura.^{6–8} In our case, the primary lesions both clinically and dermoscopically were very similar to the previously reported cases of CLL after Pfizer vaccination^{9,10} or SARS-Cov-2 infection which were, however, located on the hands and feet respectively.³ We report this particular and unusual localization of pernio-like lesions on the knees, to point out that the appearance of these type of lesions after COVID-19 vaccine cannot be considered a coincidence, also because all the patients reported in the literature had never suffered of similar lesions before facing COVID-19 or its vaccine.

The possible pathogenic mechanisms behind the association between COVID-19 or SARS-Cov-2 vaccines and purpuric or CLL lesions are unclear. Currently, the most plausible hypothesis is that Covid-19 related CLL may represent a virus-induced interferonopathy associated with a strong activation of innate immune system and fast clearance of the virus and antibodies.⁸



Figure 1 Pernio-like lesions bilaterally located on the knees and lower part of the thighs (a–b), dermoscopy examination with the typical coppery background associated with dotted vessels (c).

The appearance of purpuric and/or CLL lesions after administration of different SARS-CoV-2 vaccines seems to suggest however that these lesions could be also considered as a particular form of exanthema induced by the activation of the immune system against the viral spike protein irrespectively of its natural or synthetic origin in predisposed individuals.

Acknowledgements

The patients in this manuscript have given written informed consent to publication of their case details.

Conflicts of interest



The authors have no financial obligations or conflict of interest to declare.

Funding source

None.

Data availability statement

Data sharing is not applicable to this article, as no new data were created or analysed in this study.

A. Bassi,^{1,*}  C. Mazzatenta,¹ A. Sechi,²  M. Cutrone,³ V. Piccolo⁴

¹UO Dermatologia Lucca- Azienda USL Toscana Nordovest, Lucca, Italy,

²Dermatologic Unit, San Bortolo Hospital, Vicenza, Italy, ³Pediatrics Unit,

San Bortolo Hospital, Vicenza, Italy, ⁴Dermatology Unit, University of Campania Luigi Vanvitelli, Naples, Italy

*Correspondence: A. Bassi. E-mail: bassi76@interfree.it

References

- Piccolo V, Neri I, Manunza F, Mazzatenta C, Bassi A. Chilblain-like lesions during the COVID-19 pandemic: should we really worry? *Int J Dermatol* 2020; **59**: 1026–1027.
- Bassi A, Russo T, Argenziano G *et al.* Chilblain-Like Lesions during COVID-19 Pandemic: the State of the Art. *Life* 2021; **11**: 23.
- Català A, Muñoz-Santos C, Galván-Casas C *et al.* Cutaneous reactions after SARS-CoV-2 vaccination: a cross-sectional Spanish nationwide study of 405 cases. *Br J Dermatol* 2022; **186**: 142–152. <https://doi.org/10.1111/bjd.20639>
- Piccolo V, Bassi A, Argenziano G *et al.* Dermoscopy of chilblain-like lesions during the COVID-19 outbreak: a multicenter study on 10 patients. *J Am Acad Dermatol* 2020; **83**: 1749–1751.
- Sun Q, Fathy R, McMahon DE, Freeman EE. COVID-19 vaccines and the skin: the landscape of cutaneous vaccine reactions worldwide. *Dermatol Clin* 2021; **39**: 653–673.
- Malayala SV, Mohan G, Vasireddy D, Atluri P. Purpuric rash and thrombocytopenia after the mRNA-1273 (Moderna) COVID-19 vaccine. *Cureus* 2021; **13**: e14099.
- Sirufu MM, Raggiunti M, Magnanini LM, Ginaldi L, De Martinis M. Henoch-Schönlein purpura following the first dose of COVID-19 viral vector vaccine: a case report. *Vaccines (Basel)* 2021; **9**: 1078.
- Mazzatenta C, Piccolo V, Pace G *et al.* Purpuric lesions on the eyelids developed after BNT162b2 mRNA COVID-19 vaccine: another piece of SARS-CoV-2 skin puzzle? *J Eur Acad Dermatol Venereol* 2021; **35**: e543–e545.
- Piccolo V, Bassi A, Argenziano G *et al.* BNT162b2 mRNA COVID-19 vaccine-induced chilblain-like lesions reinforces the hypothesis of their relationship with SARS-CoV-2. *J Eur Acad Dermatol Venereol* 2021; **35**: e493–e494.
- Cameli N, Silvestri M, Mariano M, Nisticò SP, Cristaudo A. Pernio-like skin lesions after the second dose of Pfizer-BioNTech COVID-19 vaccine. *J Eur Acad Dermatol Venereol* 2021; **35**: e725–e727.

DOI: 10.1111/jdv.18025

Association between vaccination and immunobullous disorders: a brief, updated systematic review with focus on COVID-19

Editor,

Autoimmune bullous diseases (AIBDs), including the heterogeneous groups pemphigus and pemphigoid, are rare and potentially life-threatening chronic inflammatory blistering disorders characterized by autoantibodies against desmosomal adhesion proteins and structural proteins of the dermal–epidermal junction, respectively.^{1,2}

We have previously provided an overview of different vaccines against bacterial and viral infections possibly associated with the development of AIBDs, but information specifically pertaining to COVID-19 vaccines was lacking at the time of publication.³ Given the accumulating evidence of a possible association between COVID-19 vaccines and AIBDs since then, a rapid, updated systematic review focusing on this potential link was performed.

The systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Literature from the inception of the database until 09 February 2022 was explored using PubMed. Keywords were ‘pemphigus’ or ‘pemphigoid’ or ‘bullous’ or ‘blistering’ combined with ‘COVID-19 vaccination’ or ‘COVID-19 vaccine’ or ‘SARS-CoV-2 vaccination’ or ‘SARS-CoV-2 vaccine’. Additional author searches, including screening of bibliographies, were done to find further relevant publications. Inclusion criteria were peer-reviewed, English language articles about AIBD cases in association with COVID-19 vaccination. Pure reviews and basic research studies as well as articles not meeting the inclusion criteria were excluded. Collected data were checked by a second author, and any disagreement or data inconsistency were resolved by discussion.

At the end of our selection process with critical screening of titles, abstracts and full text, we included 30 papers (Fig. 1). These comprised 27 case reports/series ($n = 272$ vaccine recipients; 218 [80.1%] unspecified AIBDs, 41 [15.1%] bullous pemphigoid, 10 [3.7%] pemphigus vulgaris, 2 [0.7%] linear IgA disease and 1 [0.4%] pemphigus foliaceus), one prospective observational case–control study ($n = 8$ vaccine recipients; 8 [100%] unspecified pemphigus subtype), one registry-based