

vaccination. *J Eur Acad Dermatol Venereol* 2021; **35**: e415–e416. <https://doi.org/10.1111/jdv.17225>

- 5 Clark AK, Dhossche J, Korcheva VB, Keller JJ. Herpes zoster presenting as unilateral vasculitis. *Dermatol Online J* 2018; **24**: 13030/qt5dd717sw.

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New-onset acral lesions on hands after administration of mRNA-1273 vaccine against SARS-CoV-2: clinical images and histopathological study of three cases

Dear Editor,

First approved vaccines against SARS-CoV-2 (mRNA-1273 and BNT162b2) consists of Messenger Ribonucleic Acid (mRNA),

encoding the SARS-CoV-2 spike protein that penetrate cells and produce spike protein.¹ In these vaccines' clinical trials, chilblain-like lesions were not reported^{2,3}; however, the World Health Organization warned of the possible of appearance of chilblain-like lesions during SARS-CoV-2 vaccination campaign.⁴

On February 2021, in Salamanca (Spain), hospital workers with ages ranging between 22 and 65 years were vaccinated. All of them were advised to notify any adverse effect associated to vaccination, including cutaneous manifestations. About 150 cutaneous manifestations were notified. Three patients with new-onset of acral inflammatory lesions on hands after SARS-CoV-2 mRNA-1273 vaccine were studied. Each patient underwent complete medical history and tests to discard other aetiologies. We performed SARS-CoV-2 tests included SARS-CoV-2 anti-spike antibodies with chemiluminescence immunoassay test (CLIA), and skin biopsies to each patient. Close follow-up was set up. Second dose of SARS-CoV-2 vaccine was not contraindicated.

Two of the three patients are female and all three have ages ranging between 29 and 54 years. The three patients are hospital

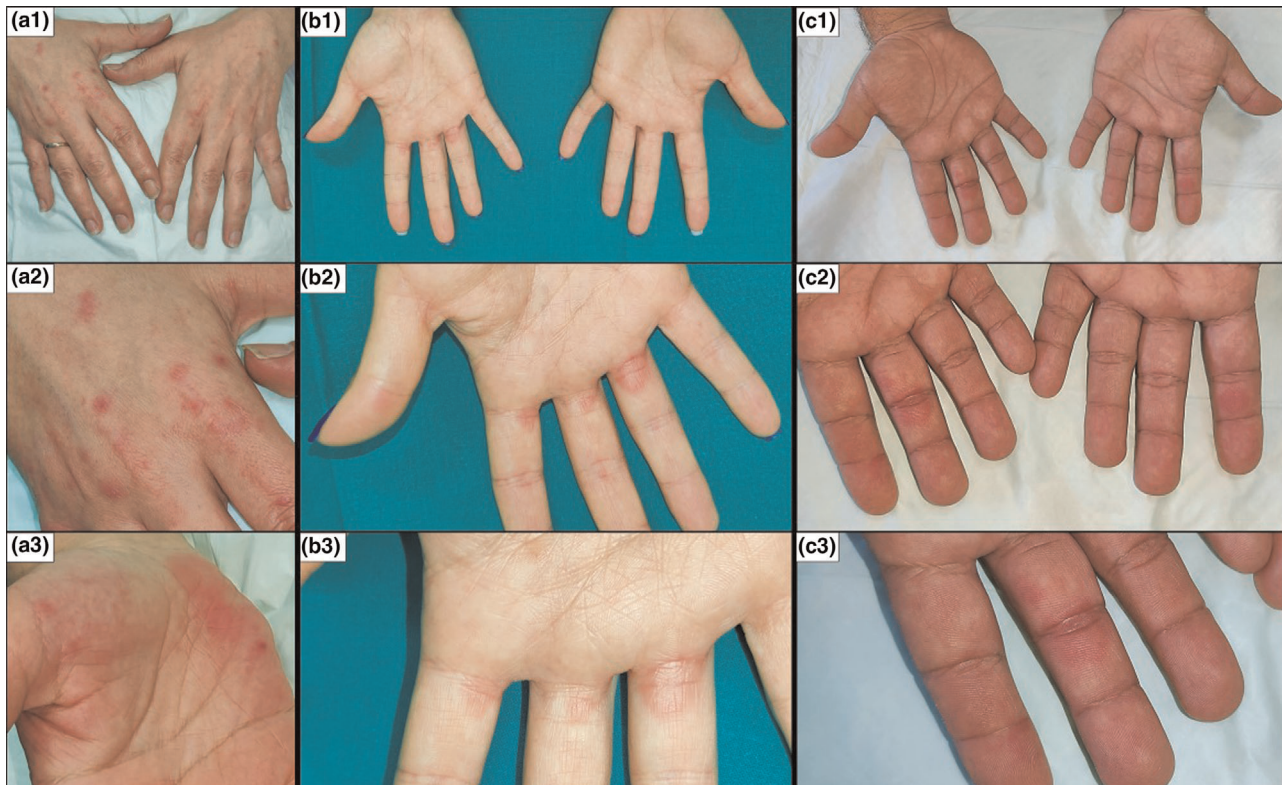


Figure 1 Clinical images of acral inflammatory lesions on the hands of the three patients. Patient 1 has itchy oedematous erythematous papules on the back of the hands and fingers (a1), mostly in the opposite hand to the vaccination arm (a2) and erythematous spots in palms (a3). The erythematous papules of this patient (a1, a2) could also be reminiscent of erythema multiforme-like lesions as well as chilblain-like lesions related to COVID-19. Patient 2 has a few similar lesions to the previous patient in the back of the hands. Patients 2 and 3 have itchy oedematous erythematous lesions in fingers (b1, b2, b3, c1, c2, c3). Most lesions in patients 2 and 3 appear on the opposite hand to the vaccination arm (b2, b3, c2, c3).

workers in SARS-CoV-2 free hospital zones. None of them have relevant medical history. All the three patients received mRNA-1273 SARS-CoV-2 vaccine and reported acral lesions on their hands between 3 and 10 days after the first dose. None had systemic symptoms. Both SARS-CoV-2 reverse transcriptase–polymerase chain reaction (RT-PCR) and SARS-CoV-2 anti-nucleocapsid antibodies CLIA test were negative in the three patients. Patient 2 and 3 had high titres for SARS-CoV-2 anti-spike antibodies (IgG). All patients received topical corticosteroids and lesions resolved in 15 days. The second dose of the vaccine had not complications or similar skin lesions. Clinical acral lesions are depicted and described in Fig. 1. Histopathological study of the lesions of each patient revealed a chilblain-like histologic pattern (Fig. 2).

We report a case-series of three patients with new-onset acral lesions on hands after administration of mRNA-1273 SARS-CoV-2 vaccine. These lesions are similar to SARS-CoV-2 chilblain-like lesions. Other aetiologies causing the lesions have been discarded given the normal values in laboratory screening tests. Although lesions appeared during the winter season, the temperatures in our district were not cold enough to think that could be simply idiopathic chilblain. Given that, no other recognizable cause for the lesions was found, and all three patients had a recent history of vaccination with mRNA-1273 SARS-CoV-2 vaccine, this is the most likely possible cause of these lesions. The three patients were able to complete vaccination doses without consequences.

Recently, isolated cases of chilblain-like after mRNA SARS-CoV-2 vaccines were reported,^{5–9} but only one have

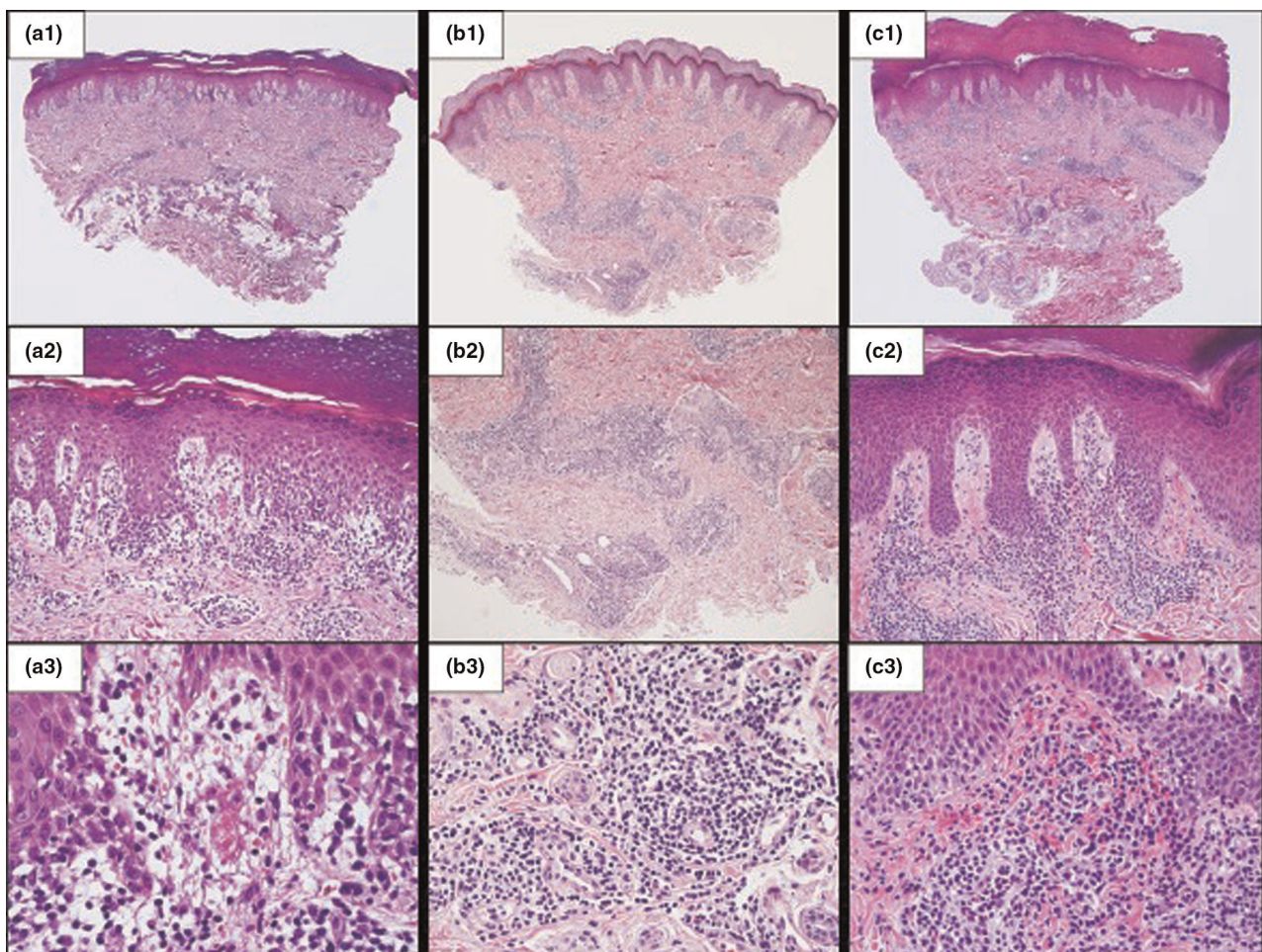


Figure 2 Histopathological images of acral inflammatory lesions on the hands in each of the three patients. Biopsies of the lesions revealed perivascular lymphocytic infiltrates with vascular damage (a1, a2, b1, b2, c1, c2) and red cell extravasation (a3, c3) in patients 1 and 3. The inflammatory infiltrate was mainly superficial but extended into the deep dermis (a1, a2, b1, b2, c1, c2), surrounding sweat glands in patient 2 (b3). Papillary dermal oedema was present in patients 1 and 2 (a2, c2). No interface dermatitis was evidenced in any patient. Lesions of all 3 patients presented a chilblain-like histology pattern.

histopathological study.⁹ Some of the cases previously reported^{6–9} describe acral lesions on hands, like in our three patients.

This is the first case-series of acral lesions, similar to chilblain-like lesions, related to SARS-CoV-2 mRNA vaccines with clinical images and histopathological study. Besides, these are the first cases of acral lesions, similar to chilblain-like lesions after mRNA vaccines against SARS-CoV-2 reported in Spain.

Both SARS-CoV-2 mRNA vaccines produce SARS-CoV-2 spike protein in the human body, and this may directly or indirectly cause endotheliitis, which could lead to the appearance of acral inflammatory lesions or chilblain-like lesions. Further studies should be carried out over the pathophysiology of chilblain-like lesions related to COVID-19 and SARS-CoV-2 vaccines.

Dermatologists and other physicians should be aware of the possible of appearance of acral inflammatory lesions associated with SARS-CoV-2 vaccines. These lesions may be more frequent on hands. As chilblain-like lesions in COVID-19 patients are more frequent in children and young people,¹⁰ more acral lesions or chilblain-like lesions associated with SARS-CoV-2 vaccines could be reported when vaccinating young people.

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Conflicts of interest

None reported.

Author contributions

Revilla-Nebreda and Roncero-Riesco had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Revilla-Nebreda and Roncero-Riesco contributed equally. *Concept and design:* Revilla-Nebreda, Roncero-Riesco, Santos-Briz. *Acquisition, analysis or interpretation of data:* All authors. *Drafting of the manuscript:* Revilla-Nebreda, Roncero-Riesco, Medina-Migueláñez, Segurado-Tostón, Santos-Briz. *Critical revision of the manuscript for important intellectual content:* All authors. *Statistical analysis:* Not applicable. *Obtained funding:* Roncero-Riesco, Santos-Briz, Román-Curto. *Administrative, technical or material support:* All authors. *Supervision:* Revilla-Nebreda, Roncero-Riesco, Santos-Briz, Román-Curto. *Other (diagnosis pathology):* Santos-Briz.

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References

- 1 Park KS, Sun X, Aikins ME, Moon JJ. Non-viral COVID-19 vaccine delivery systems. *Adv Drug Deliv Rev* 2021; **169**: 137–151. <https://doi.org/10.1016/j.addr.2020.12.008>.
- 2 Baden LR, El Sahly HM, Essink B *et al*. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med* 2021; **384**(5): 403–416. <https://doi.org/10.1056/NEJMoa2035389>.
- 3 Polack FP, Thomas SJ, Kitchin N *et al*. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med* 2020; **383**(27): 2603–2615. <https://doi.org/10.1056/NEJMoa2034577>.
- 4 World Health Organization. COVID-19 vaccines: safety surveillance manual. World Health Organization; 2020, p. 92–98. <https://apps.who.int/iris/handle/10665/338400>. License: CC BY-NC-SA 3.0 IGO. Accessed on March 7, 2021.
- 5 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. <https://doi.org/10.1016/j.jaad.2021.03.092>.
- 6 Temiz SA, Abdelmaksoud A, Dursun R, Vestita M. Acral chilblain-like lesions following inactivated SARS-CoV-2 vaccination. *Int J Dermatol* 2021; **60**: 1152–1153. <https://doi.org/10.1111/ijd.15619>.
- 7 Pileri A, Guglielmo A, Raone B, Patrizi A. Chilblain lesions after COVID-19 mRNA vaccine. *Br J Dermatol* 2021; **185**: e3. <https://doi.org/10.1111/bjd.20060>.
- 8 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. <https://doi.org/10.1111/jdv.17320>.
- 9 Kha C, Itkin A. New-onset chilblains in close temporal association to mRNA-1273 vaccination. *JAAD Case Rep* 2021; **12**: 12–14. <https://doi.org/10.1016/j.jdc.2021.03.046>.
- 10 Galván Casas C, Català A, Carretero Hernández G *et al*. Classification of the cutaneous manifestations of COVID-19: a rapid prospective nationwide consensus study in Spain with 375 cases. *Br J Dermatol* 2020; **183**(1): 71–77. <https://doi.org/10.1111/bjd.19163>.

DOI: 10.1111/jdv.17553