



Figure 2 Acro-ischæmic lesions are seen on the fingers (a), heels (b) and toes (c).

Conflict of Interests

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript.

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likely consequence of both vasculitis and coagulopathy. *J Eur Acad Dermatol Venereol* 2020; **34**: e679–e680. <https://doi.org/10.1111/jdv.16763>.

- 7 de Perosanz-Lobo D, Fernandez-Nieto D, Burgos-Blasco P *et al*. Urticarial vasculitis in COVID-19 infection: a vasculopathy-related symptom? *J Eur Acad Dermatol Venereol* 2020; **34**(10): e566–e568.s
- 8 Zhang Y, Xiao M, Zhang S *et al*. Coagulopathy and Antiphospholipid Antibodies in Patients with Covid-19. *N Engl J Med* 2020; **382**: e38.
- 9 Recalcati S. Cutaneous manifestations in COVID-19: a first perspective. *J Eur Acad Dermatol Venereol JEADV* 2020; **34**: e212–e213.
- 10 Moscarella E, Pasquali P, Cinotti E, Tognetti L, Argenziano G, Rubegni P. A survey on teledermatology use and doctors' perception in times of COVID-19. *J Eur Acad Dermatol Venereol* 2020; **34**: e772–e773.

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References

- 1 Freeman EE, McMahon DE, Lipoff JB *et al*. The spectrum of COVID-19-associated dermatologic manifestations: An international registry of 716 patients from 31 countries. *J Am Acad Dermatol* 2020; **83**: 1118–1129.
- 2 Matar S, Oulès B, Sohler P *et al*. Cutaneous manifestations in SARS-CoV-2 infection (COVID-19): a French experience and a systematic review of the literature. *J Eur Acad Dermatol Venereol* 2020; **34**: e686–e689.
- 3 Suarez-Valle A, Fernandez-Nieto D, Diaz-Guimaraens B, Santas MD, Carretero I, Garcia BP. Acro-ischæmia in hospitalized COVID-19 patients. *J Eur Acad Dermatol Venereol* 2020; **34**: e455–e457.
- 4 Ladha MA, Luca N, Constantinescu C, Naert K, Ramien ML. Approach to Chilblains during the COVID-19 pandemic. *J Cutan Med Surg* 2020; **24**: 504–517.
- 5 Simonsen U, García-Sacristán A, Prieto D. Penile arteries and erection. *J Vasc Res* 2002; **39**: 283–303.
- 6 Giudice PD, Boudoumi D, Guen BL *et al*. Catastrophic acute bilateral lower limbs necrosis associated with COVID-19 as a

Pityriasis rosea, COVID-19 and vaccination: new keys to understand an old acquaintance

Dear Editor,

Lately, we have witnessed sporadic reports of Pityriasis rosea (PR) and PR-like eruptions associated with SARS-CoV-2.¹ Such relationship has raised debate on the possible aetiopathogenic mechanism underlying this exanthematous disease. Our aim is to reinforce the link between PR and coronaviruses based on our finding of two cases following COVID-19 vaccination – the first

to our knowledge – and two cases related to SARS-CoV-2 infection.

Clinical pictures of the patients hereby reported are described in Figs 1 and 2. In all of them, morphology, distribution and evolution of skin lesions were compatible with the diagnosis of PR. The two patients with the vaccine-associated PR developed the herald patch 24 h and 7 days after the second dose of the Pfizer BioNTech vaccine (BioNTech Manufacturing GmbH, Mainz, Germany), respectively. ELISA serology revealed positive

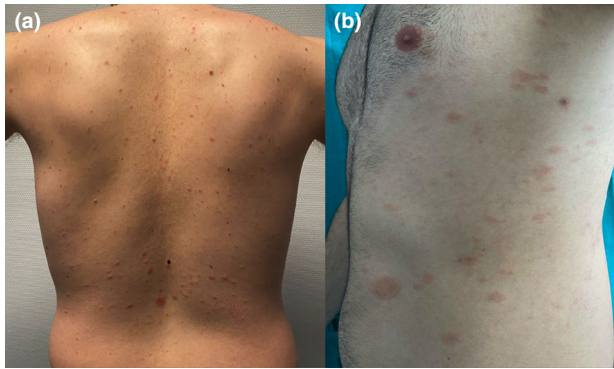


Figure 1 (a) Herald patch followed by typical oval-shaped macules appeared along skin tension lines in this 26-year-old patient seven days after the second dose of COVID-19 vaccine. Biopsy revealed mild spongiosis with foci of parakeratosis and a lymphohistiocytic infiltrate around superficial vessels. (b) This 29-year-old man presented similar findings, but the rash started 24 h after complete vaccination. RPR was non-reactive in both cases.

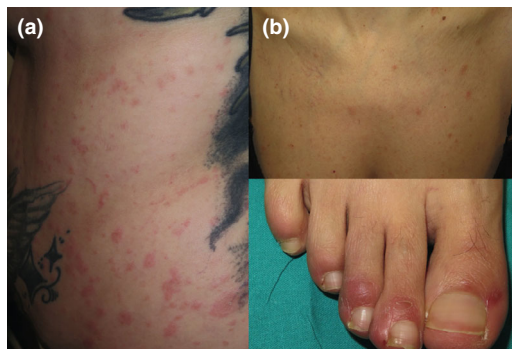


Figure 2 (a) This 26-year-old woman presented pruritic erythematous patches with mild, peripheral scaling in trunk and proximal aspects of the limbs. She had symptoms suggesting COVID-19 a month before and positive IgG antibodies. (b) This 48-year-old woman presented chilblain-like macules on the toes after a high-risk contact with an infected patient. She subsequently developed a rash suggesting PR but had no COVID-19 symptoms nor positive serology. However, SARS-CoV-2 infection was presumed based on clinical and epidemiological factors.

SARS-CoV-2 IgG antibodies in both cases. The remaining two patients recalled symptoms or signs suggesting COVID-19 in the preceding weeks, although serologic confirmation was possible in just one of them. All four patients had negative nasopharyngeal PCR test and absence of systemic symptoms at the moment of the dermatologic evaluation. We also obtained positive HHV-6 serology in three cases, with titres ranging from 1 : 160 to 1 : 640.

Aetiopathogenesis of PR has never been clarified. A viral origin was proposed based on clinical aspects (seasonal pattern and flu-like prodromal symptoms) and laboratory findings (intracellular virus-like particles, cytopathic degeneration of keratinocytes and elevation of IFN- γ).² Although multiple candidates were initially considered, the reiterated finding of DNA sequences of HHV-6/7 in plasma, skin lesions and peripheral blood mononuclear cells (PBMCs) pointed to these agents as the main aetiological factors. Positive tissue immunohistochemistry, viral mRNA in situ hybridization and neutralizing or high-avidity IgG antibodies against HHV-6/7 have also been detected in patients with PR,³ supporting the idea of an endogenous reactivation. Regression of lesions in response to acyclovir therapy strengthens that hypothesis.⁴

Nonetheless, other studies have failed to detect such findings, so PR appearing in association with COVID-19 may question the link between the former and herpesviruses. Given that HHV-6/7 reactivation might represent an epiphenomenon in the setting of immune dysregulation, a doubt arises on whether PR could be a direct manifestation of viral primoinfections, like SARS-CoV-2. The increasing number of reports relating PR to COVID-19 should also raise the question whether seasonal coronaviruses might have been the actual cause of PR cases observed in the past. However, this should not be incompatible with HHV-6 reactivation as the main aetiopathogenic pathway for PR. Drago *et al.*⁵ reported that viral DNA and high-avidity HHV-6 and EBV antibodies were detected in a case of COVID-19-related PR, suggesting that SARS-CoV-2 might have triggered a chained viral reactivation. In three of our patients, we also demonstrated high HHV-6 antibody titres, supporting this hypothesis. This phenomenon is yet to be understood but probably plays a role in other skin eruptions like drug reaction with eosinophilia and systemic symptoms.⁶ Furthermore, herpes simplex virus and cytomegalovirus reactivations have also been found in severe COVID-19 patients, and they could be related to an acquired state of immunodeficiency determined by SARS-CoV-2-associated lymphopaenia.⁷

Pityriasis rosea-like rashes have been described after H1N1 influenza, HPV, diphtheria, poliomyelitis, smallpox, pneumococcal, hepatitis B and BCG vaccinations.⁸ In some cases, antibodies against HHV-6/7 as well as viral DNA in plasma and PBMCs were detected.^{9,10} These findings suggest that immune-induced viral reactivation – rather than viral primoinfection – may be the primary cause of this disease and

not a mere epiphenomenon. Like some investigators have proposed, the elicitation of a specific immune response against an infectious agent triggered by vaccines might distract the cell-mediated control on latent infections such as HHV-6/7.⁸

The fundamentals of this immunomodulatory effect of vaccinations remain obscure and such connection can only be speculated. In spite of that, our report reinforces the idea that immune-related herpesvirus reactivation – driven by infections, vaccines, drugs or other factors – may be involved in the genesis of PR. More studies are needed to detail the pathogenic mechanisms through which this event might occur. Also, we consider that the ongoing connection between COVID-19 and PR should encourage clinicians to explore the relationship between this exanthematous disease and seasonal coronaviruses.

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References

- Ehsani AH, Nasimi M, Bigdelo Z. Pityriasis rosea as a cutaneous manifestation of COVID-19 infection. *J Eur Acad Dermatol Venereol* 2020; **34**: 436–437.
- Drago F, Ciccarese G, Broccolo F *et al*. The role of cytokines, chemokines, and growth factors in the pathogenesis of Pityriasis Rosea. *Mediators Inflamm* 2015; **2015**: 438963.
- Watanabe T, Kawamura T, Jacob SE *et al*. Pityriasis rosea is associated with systemic active infection with both human herpesvirus-7 and human herpesvirus-6. *J Invest Dermatol* 2002; **119**: 793–797.
- Rodríguez-Zuniga M, Torres N, García-Perdomo H. Effectiveness of acyclovir in the treatment of pityriasis rosea. A systematic review and meta-analysis. *An Bras Dermatol* 2018; **93**: 686–695.
- Drago F, Ciccarese G, Rebora A, Parodi A. Human herpesvirus-6, -7, and Epstein-Barr virus reactivation in pityriasis rosea during COVID-19. *J Med Virol* 2021; **93**: 1850–1851.
- Cho YT, Yang CW, Chu CY. Drug reaction with eosinophilia and systemic symptoms (DRESS): an interplay among drugs, viruses, and immune system. *Int J Mol Sci* 2017; **18**: 1243.
- Le Bal'ch P, Pinceaux K, Pronier C, Seguín P, Tadié JM, Reizine F. Herpes simplex virus and cytomegalovirus reactivations among severe COVID-19 patients. *Crit Care* 2020; **24**: 530.
- Drago F, Ciccarese G, Javor S, Parodi A. Vaccine-induced pityriasis rosea and pityriasis rosea-like eruptions: a review of the literature. *J Eur Acad Dermatol Venereol* 2016; **30**: 544–545.
- Papakostas D, Stavropoulos PG, Papafragkaki D, Grigoraki E, Avgerinou G, Antoniou C. An atypical case of pityriasis rosea gigantea after influenza vaccination. *Case Rep Dermatol* 2014; **6**: 119–123.
- Drago F, Ciccarese G, Rebora A, Parodi A. Pityriasis rosea following human papillomavirus vaccination. *Braz J Infect Dis* 2015; **19**: 224–225.

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Pityriasis rosea following CoronaVac COVID-19 vaccination: a case report

Dear Editor,

According to official data published by the World Health Organization, more than 100 million cases worldwide have been confirmed to be infected with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), causing over two million deaths. The CoronaVac vaccine, an inactivated vaccine candidate against COVID-19 containing inactivated SARS-CoV-2, is a Chinese vaccine developed by Sinovac Life Sciences (Beijing, China). Randomized, double-blind, placebo-controlled phase 1/2 clinical trials demonstrated the safety, tolerability and immunogenicity of the CoronaVac vaccine, an inactivated COVID-19 vaccine, in healthy adults 18 years of age and older.^{1,2} A branch of CoronaVac vaccine phase 3 clinical trials were conducted in Turkey. Republic of Turkey Ministry of Health General Directorate for Pharmaceuticals and Pharmacy has approved the CoronaVac COVID-19 vaccine for the emergency use of the disease on 13 January 2021.^{1,3} Vaccination was initiated in healthcare workers in our country. The adverse effects of the inactivated CoronaVac vaccine have not been fully characterized yet. Here, we report one case of pityriasis rosea in a patient following CoronaVac COVID-19 vaccination.

A 45-year-old female healthcare worker applied to our dermatology outpatient clinic for evaluation of skin rashes which developed 4 days after the first dose of CoronaVac COVID-19 vaccine and had been present for 1 week. There was no itching, and there were no accompanying systemic symptoms. She denied any history of allergies, recent infections or drug exposure, and contact with anyone with COVID 19 infection, as well as similar skin rashes in personal or family history.

Dermatological examination revealed two oval thin plaques 2 cm in diameter with a peripheral collarette scaling consistent with the herald patch on the right scapula and the right breast. There were multiple, discrete, 1–2 cm diameter, oval to round, salmon-coloured plaques over the trunk and proximal