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 fundaments 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.

Acknowledgement

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

Funding sources

None.

Conflict of interest

Nothing to disclose.

J.M. Busto-Leis,[1,*] G. Servera-Negre,[1] A. Mayor-Ibarguren,[1] E. Sendagorta-Cudós,[1] M. Feito-Rodríguez,[1] A. Nuño-González,[1] M.D. Montero-Vega,[2] P. Herranz-Pinto[1]

[1]Department of Dermatology, La Paz University Hospital, Madrid, Spain, [2]Department of Microbiology, La Paz University Hospital, Madrid, Spain

*Correspondence: J.M. Busto Leis. E-mail: josemanuel.busto@salud.madrid.org

References

1 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.

2 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.

3 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.

4 Rodriguez-Zuniga M, Torres N, Garcia-Perdomo H. Effectiveness of acyclovir in the treatment of pityriasis rosea. A systematic review and meta-analysis. *An Bras Dermatol* 2018; **93**: 686–695.

5 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.

6 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.

7 Le Balc'h P, Pinceaux K, Pronier C, Seguin P, Tadié JM, Reizine F. Herpes simplex virus and cytomegalovirus reactivations among severe COVID-19 patients. *Crit Care* 2020; **24**: 530.

8 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.

9 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.

10 Drago F, Ciccarese G, Rebora A, Parodi A. Pityriasis rosea following human papillomavirus vaccination. *Braz J Infect Dis* 2015; **19**: 224–225.

DOI: 10.1111/jdv.17301

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

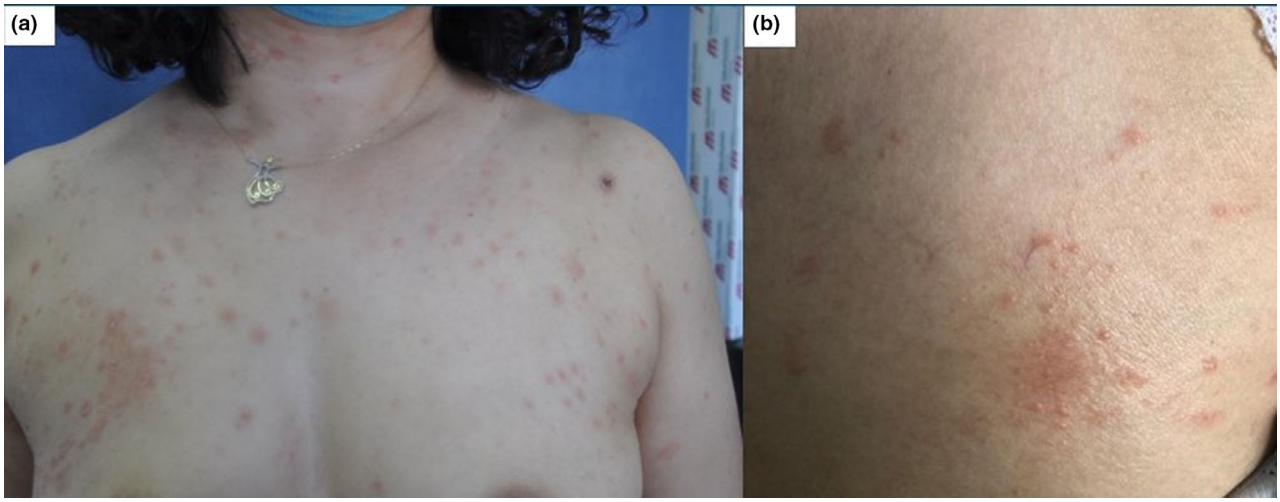

Figure 1 (a) Multiple oval salmon-coloured plaques with peripheral scales over the trunk and proximal extremities and (b) the herald patch on the right breast.

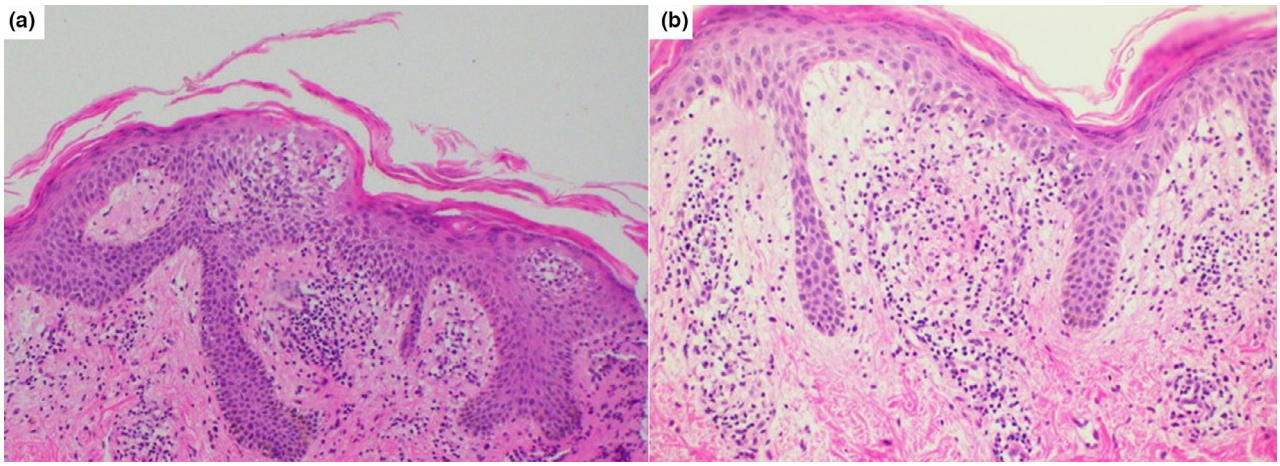

Figure 2 (a) Focal parakeratosis in mounds with exocytosis of lymphocytes and spongiosis in the epidermis (HE, ×100) and (b) extravasated red blood cells in the dermis (HE, ×200).

extremities, many of which had peripheral scales. The distribution of these plaques was along cleavage lines reminiscent of a Christmas tree pattern on the patient's body (Fig. 1). The patient had not noticed any interval between the herald patches and the diffuse rash.

Laboratory investigation did not reveal any specific abnormalities. SARS-CoV-2 PCR tests performed from both the nasopharyngeal swab sample and the skin lesion biopsy were negative.

Histopathological examination demonstrated focal parakeratosis in mounds with exocytosis of lymphocytes, spongiosis in the epidermis and extravasated red blood cells in the dermis (Fig. 2).

The patient was treated symptomatically with an oral antihistamine and a mid-potency topical corticosteroid cream and the lesions faded within 3 weeks. Twenty-eight days after the first vaccine, she received the second dose of CoronaVac COVID-19 vaccine, and 4 days after the second dose, skin rashes were similarly reactivated at the previous lesion sites and faded within a week.

According to the criteria defined by Drago *et al.*,[4] in our patient, the presence of discrete exanthematous lesions with the

herald patch without itching, absence of eosinophilia in complete blood count and histopathological findings were consistent with typical pityriasis rosea rather than pityriasis rosea-like eruptions.

Pityriasis rosea has been implicated with reactivation of human herpesviruses 6 and 7 triggered by other infections, psychological stress, pregnancy and drugs.[5] Pityriasis rosea has rarely been described after vaccines. The exact pathogenetic mechanism that leads to pityriasis rosea after vaccination is unknown.[6]

As the worldwide vaccination campaign against the COVID-19 pandemic continues, we emphasize that pityriasis rosea can result from new CoronaVac COVID-19 vaccine, for both physicians and patients, and lesions may be reactivated after the second vaccination. However, pityriasis rosea is a self-limiting benign exanthema and does not require interruption of the vaccination programme for life-threatening SARS-CoV-2 infection, but close monitoring of the skin eruptions is required.

Acknowledgement

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

Conflict of interest

Nothing to disclose.

E. Akdaş,[1,*] N. İlter,[1] B. Öğüt,[2] Ö. Erdem[2]

[1]Department of Dermatology, Faculty of Medicine, Gazi University, Ankara, Turkey, [2]Department of Pathology, Faculty of Medicine, Gazi University, Ankara, Turkey

*Correspondence: E. Akdaş. E-mail: mdelcinakdas@gmail.com

References

1 Zhang Y, Zeng G, Pan H *et al*. Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine in healthy adults aged 18–59 years: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial. *Lancet Infect Dis* 2020.**21**: 181–192.

2 Wu Z, Hu Y, Xu M *et al*. Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine (CoronaVac) in healthy adults aged 60 years and older: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial. *Lancet Infect Dis* 2021. https://www.thelancet.com/action/showPdf?pii=S1473-3099%2820%2930987-7.

3 Mallapaty S. China COVID vaccine reports mixed results—what does that mean for the pandemic? *Nature News* 2021; **15**. https://www.nature.com/articles/d41586-021-00094-z.

4 Drago F, Ciccarese G, Parodi A. Pityriasis rosea and pityriasis rosea-like eruptions: how to distinguish them? *JAAD Case Rep* 2018; **4**: 800–801.

5 Drago F, Broccolo F, Rebora A. Pityriasis rosea: an update with a critical appraisal of its possible herpesviral etiology. *J Am Acad Dermatol* 2009; **61**: 303–318.

6 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.

DOI: 10.1111/jdv.17316

BNT162b2 mRNA COVID-19 vaccine-induced chilblain-like lesions reinforces the hypothesis of their relationship with SARS-CoV-2

Dear Editor,

We have recently observed a 41-year-old woman who developed chilblain-like lesions (CLL) soon after the second administration of Pfizer (New York, NY, USA) BNT162b2 mRNA COVID-19 Vaccine. The lesions occurred exclusively on the volar aspects of the second and the third fingertip of right hand (Fig. 1). The latency between the administration of the second dose of vaccine and the occurrence of CLL was 24 h. The lesions were extremely painful. History for similar lesions was negative. The patient was otherwise healthy, and her blood examination was within normal ranges except for high levels of IgG anti-spike antibodies, thus determining the positive response to the vaccine. Molecular swab for SARS-CoV-2 showed a negative result.

After an initial phase of confusion and disagree among researchers, CLL are nowadays considered a highly likely immune-mediated reaction to SARS-CoV-2 usually observed in healthy asymptomatic young people, whose COVID status is often unremarkable.[1–6] It has been postulated that this apparent contradiction could be explained as virus-induced interferonopathy associated with a strong activation of innate immune system and fast clearance of antibodies.[7,8]

Recently, Davido *et al*.[9] reported a similar case in a 41-year-old woman developing 'blue toes' after BNT162b2 mRNA COVID-19 vaccine. Differently from our case, the patient developed CLL 4 days after the first dose of the vaccine, leading to avoid the second dose for safety reasons. Another minor difference was related to the location (toes vs. fingers). Pain was as impactful as in our patient, in contrast to what was seen in adolescents, whose CLL were often asymptomatic or poorly symptomatic (itch or mild pain), although sometimes patients complain about intense pain.

This is so the second European case of COVID vaccine-induced CLL and the first in Italy. As the number of vaccinated people is still limited, the amount of similar cases is expected to increase over time.

A clinical overlap does exist with the non-vaccine-associated CLL, and it seems obvious to think that a relationship with the vaccine is actually present.

Chilblain-like lesions are still considered an enigmatic sign, whose association with COVID-19 is a matter of debate. However, the parallel 'epidemic' of CLL contemporary to COVID-19 pandemic is one of the major proofs of their correlation.

Basically, it is very important to report postmarketing reactions to vaccines. In the specific case, Pfizer BNT162b2 mRNA

