LETTER TO THE EDITOR

Sweet Syndrome following SARS-CoV-2 CoronaVac vaccine

Editor,

A 65-year-old woman presented with febrile acute skin eruption developed 8 h after the first dose of the CoronaVac vaccine (Sinovac Life Sciences, Beijing, China). The patient had no history of SARS-CoV-2 infection. She denied any recent drug exposure, or a weight loss or previous similar eruption. Physical examination revealed fever at 39°C associated with well demarcated, oval, tender plaques on the hands and feet (Fig. 1). We also noted bilateral purplish oedematous plaques on metacarpophalangeal, distal and proximal interphalangeal joints and in the palms. Soles were affected with chilblain-like lesions. Mucous membranes were not involved. No other extracutaneous symptoms were noted. Laboratory tests showed leucocytosis with neutrophilia (86% of total leucocyte count equal 9560/mm^3 (N < 7500/mm^3)) and elevated inflammatory biomarkers including C-reactive protein (CRP) of 42.3 mg/L (Normal (N) < 3 mg/L) and ESR of 60 mm/h (N < 20 mm/h). Liver and kidney function tests were normal. Histopathology showed a marked oedema in the papillary dermis associated with a diffuse neutrophilic dermal infiltrate with marked leucocytoclasia (Fig. 2). The clinical presentation and the histopathological examination of skin biopsy were compatible with the diagnosis of SS. Chest X-ray and abdominal ultrasound examination did not show any abnormalities. Serological tests for viral and bacterial infections including Cytomegalovirus, Epstein–Barr virus, Chlamydia and Mycoplasma were negative. Antinuclear antibodies were negative. Thus, we suggested the diagnosis of COVID-19 vaccine inducing Sweet Syndrome (SS). The clinical and biological abnormalities improved within 10 days after treatment with high potency topical steroids for 15 days. One month later, after complete resolution of skin eruption, the patient underwent patch tests with pure CoronaVac vaccine on both healed and normal skin. Readings after 72 h and 5 days were negative. Intradermal tests were carried out with the same vaccine (pure and diluted at 1/10 in 0.9% saline). The immediate reading at 20 min and delayed readings at 10 h, day (D) 2 and D3 were all negative. SARS-CoV-2 antibody tests evaluated 4 weeks after the first dose of the vaccine showed undetectable level of IgG and IgM anti-COVID-19 antibodies, suggesting absence of immunization.

We authorized the administration of the second dose of CoronaVac vaccine under clinical control. The patient tolerated the second dose without developing neither adverse events nor recurrence of SS.

We reported the fifth published case of COVID-19 vaccine inducing SS and the first case to be induced by an inactivated SARS-CoV-2 vaccine 'CoronaVac'. SS can be triggered by many factors such as infections, malignancies and some drugs.[1] The

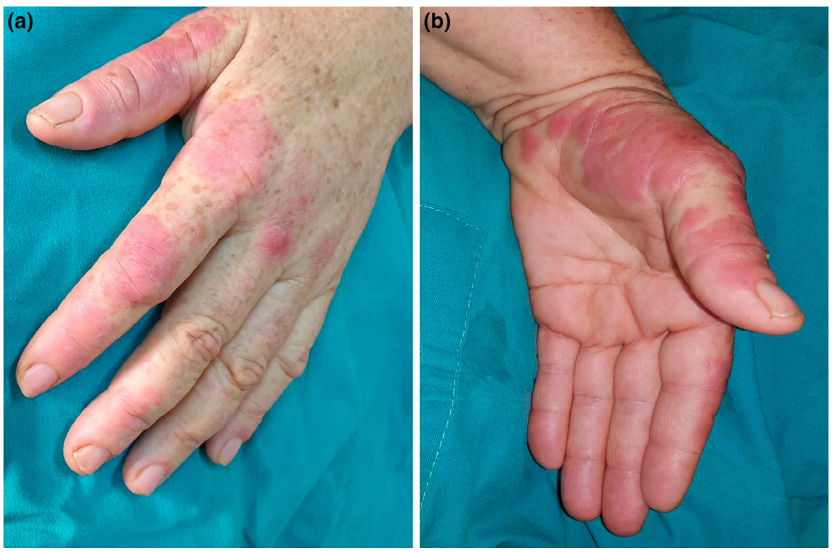

Figure 1 Tender plaques on the hands.

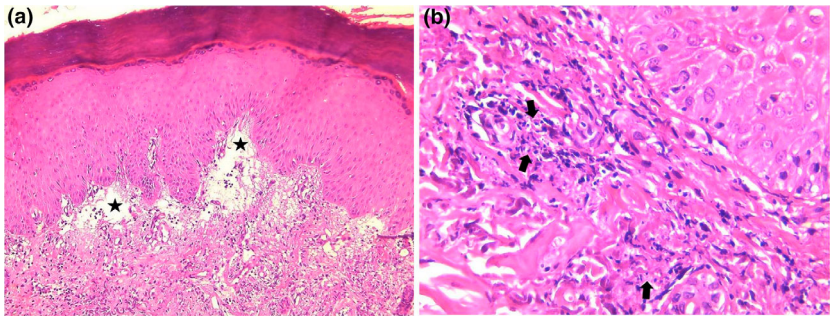

Figure 2 (a) Marked oedema in the papillary dermis (star) (H&E ×200). (b) Diffuse neutrophilic dermal infiltrate with marked leucocytoclasia (arrow) (H&E ×400).

occurrence of SS in the context of a COVID-19 infection was also reported.[1] There are some reports of SS occurring after vaccinations including seasonal influenza vaccine, H1N1 vaccine, pneumococcal vaccine and Bacille Calmette-Guerin, as well as smallpox vaccine.[2,3] To the best of our knowledge, only four cases of SS after COVID-19 vaccines have been reported and no case of SS induced by CoronaVac vaccine has been reported.[4] Two of them, like in our case, had only cutaneous involvement and were related to the SARS-CoV-2 Pfizer-BioNTech mRNA vaccine.[4] The two other cases displayed extracutaneous manifestations such as polymyositis, arthritis, acute encephalitis and myoclonus and were associated with ChAdOx1 nCoV-19 vaccine (Oxford-AstraZeneca) and Moderna mRNA-vaccine.[4] Our case is particular to have the shortest latency period between the vaccine and the skin eruption while in the other cases this period was between 24 and 96 h. This short latency time strongly supports the pathogenic role of the vaccine as a cause of SS in our case.

The physiopathology of SS following vaccination remains unknown. It seems to be related to a hypersensitivity reaction, leading to the secretion of cytokines and activation of neutrophils. As a result, the release of cytokines can cause inflammation and tissue damage. In addition, SS induced by COVID-19 vaccination may be related to the vaccine or the adjuvant which is aluminium hydroxide for CoronaVac vaccine. Patch-tests with aluminium hydroxide was not performed; in our case, on one hand the patch-test with CoronaVac vaccine was negative, and on the other hand, based on the study of Wolfson *et al.*,[5] excipient skin tests may be of little utility in assessing allergic reactions to COVID-19 vaccine, mainly in patients without anaphylaxis. In our case, the intradermal testing was negative suggesting that CoronaVac vaccine can be tested with its undiluted form as reported with Pfizer-BioNtech SARS-CoV-2 vaccine.[5] Moreover, in accordance with the study of Marcelino *et al.*,[6] through our case, we highlight the question of the exact positive predictive value of these tests and the concentration to use for interadermal tests with COVID-19 vaccines. Finally, the recurrence of SS after the second dose of COVID-19 vaccine is not systematic. So, this reaction with only skin involvement, as well as in our patient, should not forbid the second dose.

Acknowledgements
None.

Conflict of interest
None declared.

Funding source
None.

Informed consent
Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

Data availability statement
Data sharing not applicable - no new data generated, or the article describes entirely theoretical research.

N. Ben Salah,[1,*] M. Korbi,[1] N. Ben Fadhel,[2] I. Safa,[1] F. Chad,[2] M. Njima,[3] H. Belhadjali,[1] M. Amri,[1] K. Aouam,[2] J. Zili[1]

[1]Dermatology Department, Dermo-Respiratory Research Laboratory UR14 SP 03, Fattouma Bourguiba Hospital, University of Medicine, Monastir, Tunisia, [2]Pharmacology Department, Fattouma Bourguiba Hospital, University of Medicine, Monastir, Tunisia, [3]Anatomopathology Department, Fattouma Bourguiba Hospital, University of Medicine, Monastir, Tunisia

*Correspondence: N. Ben Salah. E-mail: nesrinebensalah2612019@gmail.com

References
1 Taşkın B, Vural S, Altuğ E *et al.* COVID 19 presenting with atypical sweet's syndrome. *J Eur Acad Dermatol Venereol* 2020; **10**: 534–535.
2 Jovanović M, Poljacki M, Vujanović L, Duran V. Acute febrile neutrophilic dermatosis (Sweet's syndrome) after influenza vaccination. *J Am Acad Dermatol* 2005; **52**: 367–369.

3 Hali F, Sbai M, Benchikhi H, Ouakadi A, Zamiati S. Sweet's syndrome after H1N1 influenza vaccination. *Ann Dermatol Venereol* 2010; **137**: 740–741.
4 Baffa ME, Maglie R, Giovannozzi N *et al*. Sweet syndrome following SARS-CoV2 vaccination. *Vaccine* 2021; **9**: 1212.
5 Wolfson AR, Robinson LB, Li L *et al*. First dose mRNA COVID-19 vaccine allergic reactions: limited role for excipient skin testing. *J Allergy Clin Immunol Pract* 2021; **9**: 3308–3320.
6 Marcelino J, Farinha S, Silva R *et al*. Nonirritant concentrations for skin testing with SARS-CoV-2 mRNA vaccine. *J Allergy Clin Immunol Pract* 2021; **9**: 2476–2477.

DOI: 10.1111/jdv.18336