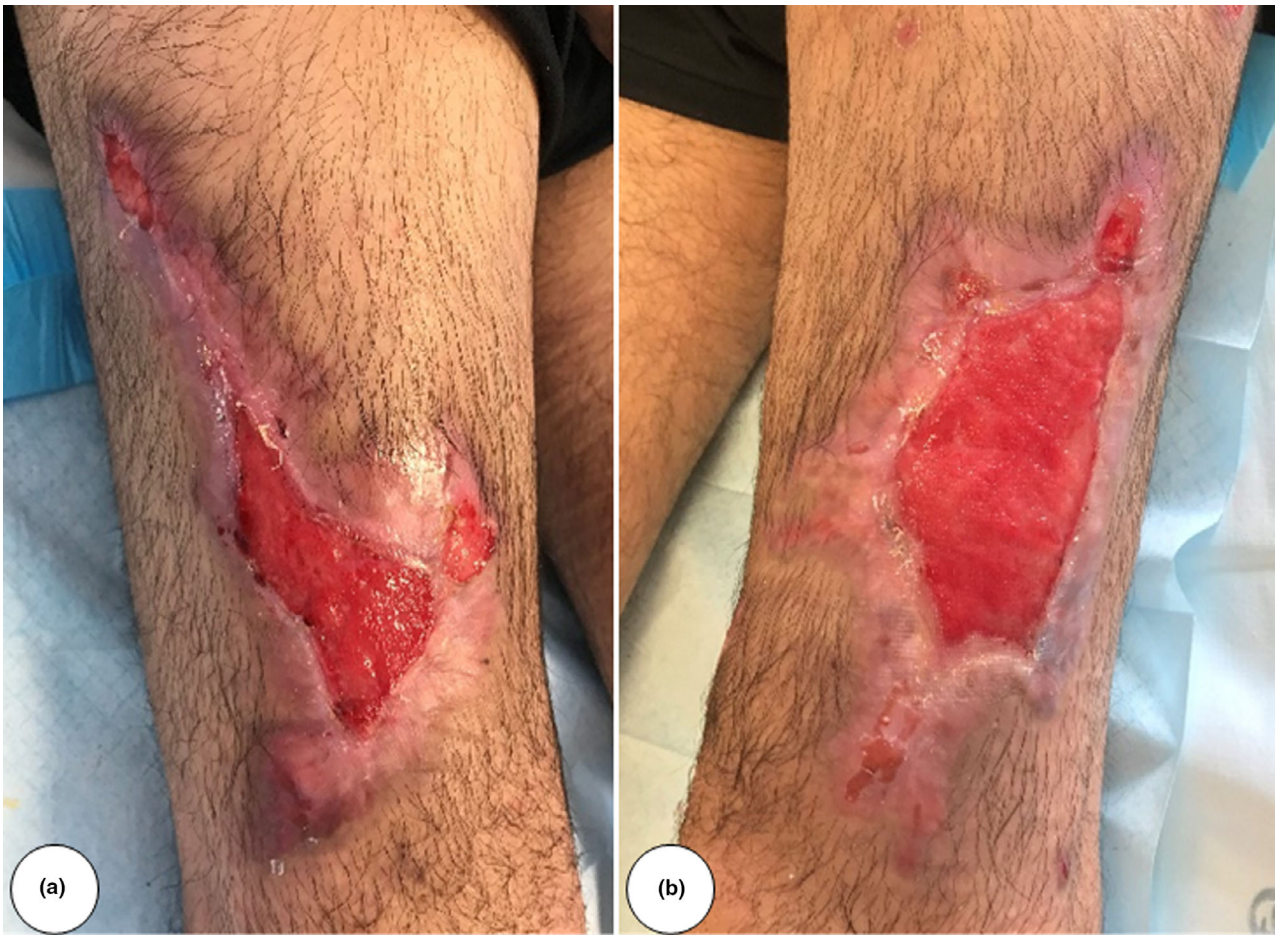


**Figure 2** Skin findings at 6 weeks of treatment, showing central ulcer with granulation tissue and surrounding epithelization area and wound contraction, maintaining original configuration. (a) Lateral aspect of the right thigh and (b) lateral aspect of the left thigh.

## References


1 Genovese G, Moltrasio C, Berti E, Marzano AV. Skin Manifestations associated with COVID-19: current knowledge and future perspectives. *Dermatology* 2021; **237**: 1–12.
2 Avila J, Long B, Holladay D, Gottlieb M. Thrombotic complications of COVID-19. *Am J Emerg Med* 2021; **39**: 213–218.
3 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**: 71–77.
4 Çabuk FK, Sakiz D. Necrotizing skin findings in coronavirus disease 2019: a case report. *Iran J Pathol* 2021; **16**: 79–83.
5 Becker RC. COVID-19-associated vasculitis and vasculopathy. *J Thromb Thrombolysis* 2020; **50**: 499–511.
6 Magro CM, Mulvey JJ, Laurence J *et al*. The differing pathophysiologies that underlie COVID-19-associated perniosis and thrombotic retiform purpura: a case series. *Br J Dermatol* 2021; **184**: 141–150.
7 Wysong A, Venkatesan P. An approach to the patient with retiform purpura. *Dermatol Ther* 2011; **24**: 151–172.
8 Bosch-Amate X, Giavedoni P, Podlipnik S *et al*. Retiform purpura as a dermatological sign of coronavirus disease 2019 (COVID-19) coagulopathy. *J Eur Acad Dermatol Venereol* 2020; **34**: e548–e549.
9 García-Irigoyen A, Acatitla-Acevedo GA, Barrera-Godínez A, Méndez-Flores S, Domínguez-Cherit J. Follow-up of dermatological manifestations in non-critical hospitalized patients with COVID-19 pneumonia and their prognostic correlation with disease severity. *J Eur Acad Dermatol Venereol* 2021; **35**: e421–e423.


DOI: 10.1111/jdv.17562

# Cutaneous reactions to inactivated SARS-CoV-2 vaccine and ChAdOx1-S (recombinant) vaccine against SARS-CoV-2: a case series from the Philippines

*Dear Editor,*

The Philippines remains one of the countries with the highest number of new COVID-19 cases in the Western Pacific region.[1]

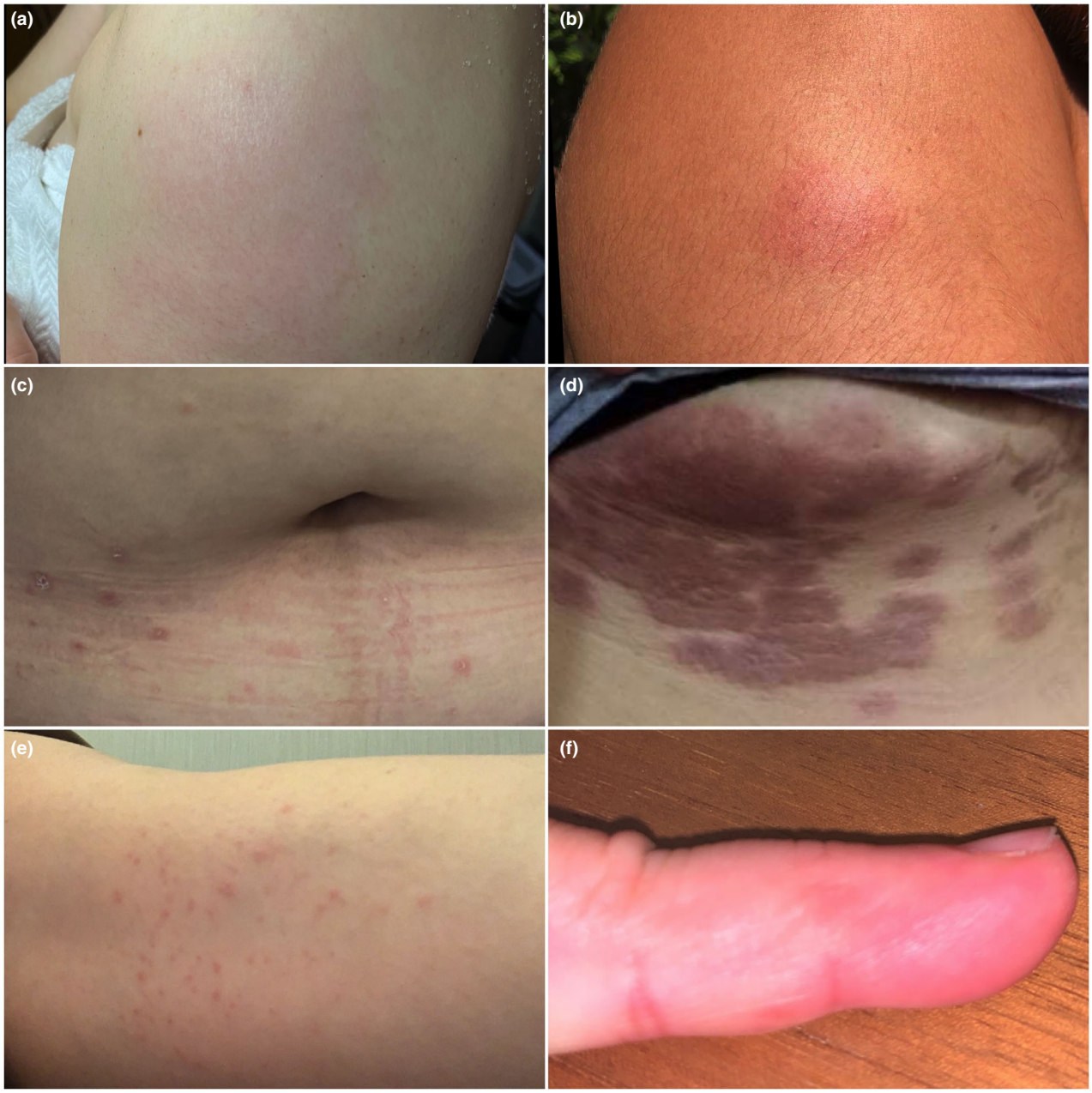


**Figure 1** Cutaneous reactions to COVID-19 vaccines. Erythematous patches on the injection site (a-b). Erythematous papules and plaques with collarette scaling on the trunk (c). Purpuric patches on the right inframammary area contralateral to the injection site (d). Erythematous macules and papules inner arm of the injected arm (e). Pruritic vesicles on the lateral aspects of the 5th digit of the injected arm (f).

The Philippine government granted emergency use authorizations for inactivated SARS-COV-2 (Sinovac) and recombinant ChAdOx1-S (AstraZeneca) vaccines. Early trials of these vaccines have described reactions ranging from injection site reactions[2,3] to generalized urticaria.[3]

We report 20 healthcare workers who developed cutaneous reactions after receiving their first dose of either Sinovac or AstraZeneca from 1 March 2021 to 31 March 2021. Seven patients received Sinovac, while 13 patients received AstraZeneca. Their median age was 37 years (range: 24–57 years).

**Table 1** Cutaneous reactions to AstraZeneca and Sinovac vaccines distant to the injection site: characteristics, associated signs and symptoms, and management

| Distant site reactions | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Patient** | **Age/ Sex** | **COVID-19 Vaccine** | **Allergy History** | **Onset postvaccination** | **Duration of reaction** | **Cutaneous reactions and associated signs and symptoms** | **Management** |
| 1 | 57/F | SV | Peanuts,<br>shrimp paste,<br>NSAIDs, aspirin,<br>cotrimoxazole,<br>prednisolone + chlorphenamine maleate | 15 min | <1 d | Angioedema on the left eye and left earlobe<br>Metallic taste, lip numbness<br>9 h postvaccination: wheals developed on the left side of the neck, associated with a coughing spasm | Betamethasone + Loratadine<br>Cetirizine |
| 2 | 54/M | SV | Etoricoxib<br>Allopurinol | 1–2 h | 1 d | Petechiae on the chest and abdomen (20% TBSA)<br>Laryngeal spasm, hoarseness, dizziness | IM epinephrine<br>IM diphenhydramine<br>Methylprednisolone<br>Bilastine |
| 3 | 29/F | AZ | None | 3 h | 3 d | Angioedema on the upper lip<br>Fever, myalgia, arthralgia<br>1-day postvaccination: angioedema on the upper lip, hoarseness, shortness of breath | IM epinephrine<br>IM diphenhydramine<br>Bilastine |
| 4 | 54/F | AZ | None | 15 min | 14 d | Wheals on both arms and legs | Cetirizine<br>Hydrocortisone cream |
| 5 | 36/M | SV | None | <30 min | 3 d | Macules and patches, generalized<br>(80% TBSA) | Cetirizine |
| 6 | 54/F | SV | Shellfish | 5 h | <1 h | Angioedema on both 2nd digits, generalized pruritus<br>Elevated BP, tachypnoea, right upper arm weakness, slurring of speech | IV hydrocortisone,<br>IM diphenhydramine<br>Betamethasone + loratadine |
| 7 | 25/F | SV | None | Day 1 | 1 d | Wheals on arms and legs with burning sensation, angioedema on the wrist, dermatographism<br>Injection site pain and numbness | IM diphenhydramine<br>Prednisone<br>Bilastine<br>Ebastine +betamethasone |
| 8 | 28/F | AZ | Ceftriaxone | Day 1 | 14 d | Purpuric patches on the right inframammary area spreading to the left with a needle-prick sensation<br>Injection site tenderness, arm pain and heaviness | Clobetasol propionate |
| 9 | 53/F | SV | Penicillin<br>NSAIDs | Day 1 | 14 d | Vesicles on ipsilateral* $^{5th\ digit,}$<br>macules and papules on ipsilateral* arm, axilla and chest, severe pruritus on ipsilateral* arm on the day of vaccination | Prednisone<br>Loratadine, cetirizine<br>Clobetasol |
| 10 | 47/F | AZ | Nalbuphine | Day 2 | 2 d | Macules on ipsilateral arm and upper chest (5% TBSA)<br>Arm pain, myalgia | Bilastine |
| 11 | 24/F | AZ | None | Day 3 | 14 d | Pityriasis rosea-like eruption on trunk and extremities with pruritus<br>Injection site pain and heaviness | Cetirizine<br>Betamethasone valerate |
| 12 | 37/F | AZ | Shrimps | Day 3 | 4 d | Erythematous macule on injection site, angioedema on the right eye<br>Arm pain and heaviness, runny nose, fever, headache, increase blood pressure | Prednisone<br>Cetirizine |
| 13 | 31/F | SV | None | Day 4 | 7 d | Erythematous macules and patches on trunk, axillae, inguinal areas (18% TBSA)<br>Headache, fever before the cutaneous eruption | Bilastine |

AZ, AstraZeneca; SV, Sinovac; and d, day *Ipsilateral to the vaccination site

Fifteen (75%) were female, and five (25%) were male. All patients were seen by either the authors or other dermatologists. All seven patients who developed localized injection site reactions received AstraZeneca (Fig. 1a,b). These were all delayed reactions, appearing more than 24 h postvaccination, and none reported symptoms of anaphylaxis. Of the 13 patients who developed distant site reactions, defined as cutaneous reactions that are distributed beyond the injection site, six received AstraZeneca, and seven received Sinovac. Six patients developed immediate cutaneous reactions: three who either had urticaria, angioedema or petechiae had anaphylactic symptoms; one experienced angioedema and transient focal neurologic deficits; and two had generalized macules and patches and urticaria but without anaphylactic symptoms. Other cutaneous reactions that appeared more than 24 h postvaccination included urticaria, angioedema, erythematous macules, patches, papules, vesicles, purpuric patches and pityriasis rosea (PR)-like eruption (Table 1; Fig. 1c-f).

Hypersensitivity to vaccines is often caused by excipients rather than the vaccine antigen. For AstraZeneca, the most likely cause is polysorbate,[4] whereas, for Sinovac, aluminium hydroxide may be causative.[3] Both have been implicated in hypersensitivity reactions.[4] Most vaccination reactions are classified as type I (immediate) or type IV (delayed) hypersensitivity responses. Type I responses usually occur within the first four hours and result from mast cell activation and degranulation, exemplified by anaphylaxis. Type IV responses are delayed, commonly within hours or days after exposure.[5] In our cases, the onset of localized injection site reactions was suggestive of type IV hypersensitivity. These were similarly reported in other mRNA vaccines.[6,7] The distant site reactions were either immediate or delayed. Three of the six patients who had immediate cutaneous reactions had anaphylactic symptoms either concomitantly or within hours. While urticaria and angioedema are common in anaphylactic reactions, the petechial rash was notable in one of our cases. None of those who had delayed cutaneous reactions developed anaphylactic symptoms. A PR-like eruption, previously reported following vaccination (Moderna and Pfizer COVID-19 vaccines, as well as influenza and hepatitis vaccines) and COVID-19 infection, may be related to a T-cell mediated response to the viral epitope rather than HHV-6 and HHV-7 reactivation associated with true PR.[7–10]

Most cutaneous reactions observed in this case series were self-limited. However, for patients presenting with immediate cutaneous reactions within hours postvaccination, it may be prudent to monitor for further development of anaphylactic symptoms in the next 24 h for immediate control and intervention. For those presenting with cutaneous reactions 24 h postvaccination, supportive management and reassurance seem sufficient. As the widespread vaccination of COVID-19 vaccines continues worldwide, we anticipate more data regarding their side effect profile, including the mechanism and pathophysiology of such side effects. The benefits versus risks from the vaccines support their use and significant role in putting an end to the pandemic.

## Acknowledgements

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

## Conflict of interest

The authors declare no conflicts of interest.

## Funding sources

None.

## IRB approval status

Not applicable.

J.N. Yu,[1,*] C.B. Angeles,[2] H.G. Lim,[3] C. Chavez,[4] C. Roxas-Rosete[4]

[1]Skin and Cancer Foundation, Inc., Pasig, Philippines, [2]University of the East Ramon Magsaysay Memorial Medical Center, Quezon City, Philippines, [3]Cebu Institute of Medicine, Cebu City, Philippines, [4]Rizal Medical Center, Pasig, Philippines

*Correspondence: J.N. Yu. E-mail: jonnevinyu@gmail.com

## References

1 World Health Organization. Coronavirus Disease 2019 (COVID-19) External Situation Report #46 [Internet]. 2021. Available from: https://www.who.int/westernpacific/internal-publications-detail/covid-19-situation-report-for-the-western-pacific-region-46-17-march-2021---23-march-2021

2 Ramasamy MN, Minassian AM, Ewer KJ *et al*. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial. *Lancet* 2020; **396**: 1979–1993. Available from https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32466-1/fulltext

3 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* 2021; **21**: 181–192. https://doi.org/10.1016/S1473-3099(20)30843-4

4 Kounis NG, Koniari I, de Gregorio C *et al*. Allergic reactions to current available COVID-19 vaccinations: pathophysiology, causality, and therapeutic considerations. *Vaccines* 2021; **9**: 221. https://doi.org/10.3390/vaccines9030221

5 McNeil MM, DeStefano F. Vaccine-associated hypersensitivity. *J Allergy Clin Immunol* 2018; **141**: 463–472. https://doi.org/10.1016/j.jaci.2017.12.971

6 Wei N, Fishman M, Wattenberg D, Gordon M, Lebwohl M. "COVID arm": a reaction to the Moderna vaccine. *JAAD Case Reports* 2021; **10**: 92–95. https://doi.org/10.1016/j.jdcr.2021.02.014

7 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**: 46–55. https://doi.org/10.1016/j.jaad.2021.03.092

8 Cyrenne BM, Al-Mohammedi F, DeKoven JG, Alhusayen R. Pityriasis rosea-like eruptions following vaccination with BNT162b2 mRNA COVID-19 Vaccine. *J Eur Acad Dermatol Venereol* 2021; **35**: e546–e548. https://doi.org/10.1111/jdv.17342

 

9 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.
10 Chen JF, Chiang CP, Chen YF, Wang WM. Pityriasis rosea following influenza (H1N1) vaccination. *J Chinese Med Assoc* 2011; **74**: 280–282.

DOI: 10.1111/jdv.17575

# Herpes zoster after ChAdOx1 nCoV-19 vaccine: a case series

*Dear Editor,*

The SARS-CoV-2 pandemic has plagued the world over the year. Many vaccines have been created to alleviate the morbidity and mortality associated with COVID-19 and stop viral transmission. In Italy, the vaccination campaign with the recombinant adenoviral vector encoding the SARS-CoV-2 spike protein (AstraZeneca) started on 30 January 2021. The most described vaccine-related side effects in the literature are fever, redness, pain and tenderness at the injection site, musculoskeletal pains and headache.[1] Here, we report three cases of patients that presented a reactivation of herpes zoster after the first dose of the vaccine (AstraZeneca).

In the first case, a 76-year-old woman presented to our dermatology department with tense vesicular lesions on an erythematous background placed on the right breast region. During anamnesis collection, it emerged that the patient received the first dose of the ChAdOx1 nCoV-19 vaccine 7 days before the skin eruption. In the second case, a 79-year-old man presented the same manifestations placed over the right thigh 6 days after vaccination. Finally, a 70-year-old man showed the same manifestations located on the left side of the neck 10 days after vaccination. None of the 3 aforementioned cases had other symptoms associated with the rash. On dermatological physical examination, groups of tense vesicles, sometimes excoriated, on an erythematous background with dermatomal distribution have been objectives, with associated burning and itching symptoms (Fig. 1). Based on the clinical history and physical examination, a diagnosis of herpes zoster was made, and, according to guidelines, systemic antiviral therapy was prescribed in all cases resulting in the resolution of the manifestations.

VZV is a DNA virus responsible for chickenpox, with a strong tropism for central nervous system cells. After the first infection, it remains latent in the cranial nerves or dorsal root ganglia. In situations of immunosuppression, trauma and fever, it can reactivate and cause shingles. The immune status of the host influences the natural history of herpes zoster. Moreover, age-related immunosenescence is the major risk factor, with the disease-related or iatrogenic immunosuppression as possible triggers for reactivation. As already described in the literature, infection with COVID-19 can trigger a VZV reactivation, too.[2] SARS-COV-2 infection probably causes an immunosuppressive state secondary to a decrease in the quantity of T lymphocytes. This immunosuppressive state has also been shown to be responsible for reactivating other viruses, such as pityriasis rosea.[3]

Moreover, as already described in the literature, vaccines can also trigger the reactivation of shingles.[4] Generally, the latency time is about 5 days, while in our experience, the mean latency of VZV reactivation after the ChAdOx1 nCoV-19 vaccine was 7.6 days. Probably, the vaccine may cause some immunomodulation that allows VZV to escape from its latent phase.[4,5] However, based on these data, it is possible to imagine that mass vaccination on a global scale, due to the Covid19 pandemic, could naturally cause an increase in the number of shingles reactivation, especially in the elderly population. As there are still very few cases of this type described in the literature, it is essential to stress how much is still to be discovered regarding the pathophysiological mechanisms underlying the dermatological manifestations after the ChAdOx1 nCoV-19 vaccine, so we find these observations noteworthy.

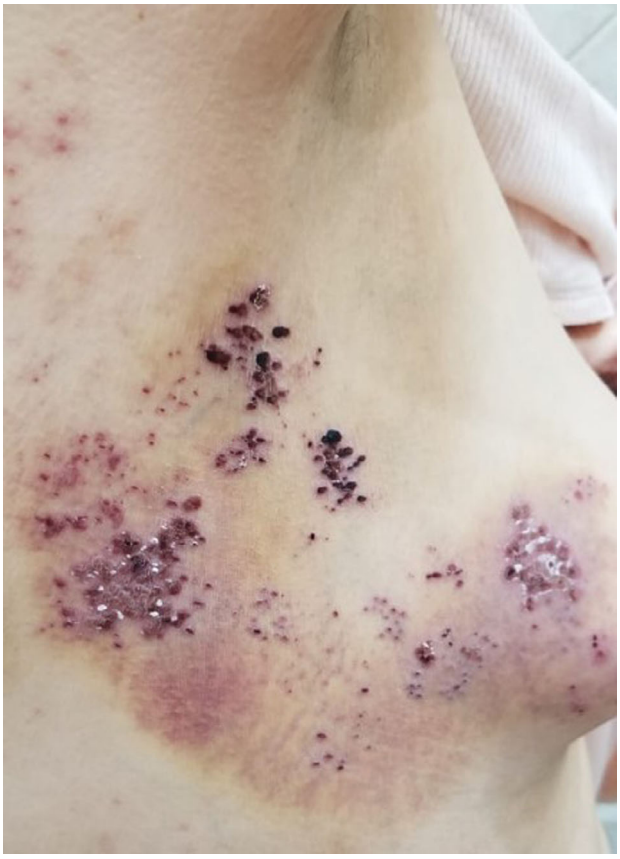

**Figure 1** Tense vesicles and serocrust located on the right breast on an erythematous background with dermatomal distribution.