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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.

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

Conflict of interest

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Herpes zoster after inactivated SARS-CoV-2 vaccine in two healthy young adults

Dear editor,

Coronavirus disease 2019 (COVID-19) can cause various cutaneous manifestations that were identified since the outbreak.¹ With the era of vaccination, cutaneous side effects of vaccines will likely be frequently encountered. Mild reactions like localized redness and swelling have been detected in vaccines reaching phase 3 trials; besides, rarer adverse effects such as injection site urticaria, maculopapular rash, reaction to dermal fillers due to COVID-19 vaccines have been reported.² COVID-19 vaccine-associated herpes zoster (HZ) has been described for the two

most used vaccine types recently: Bostan and Yalici-Armagan reported a 78-year-old man with thoracic HZ after administration of an inactivated vaccine, and Tessa and Kluger reported a 44-year-old man with cervical HZ after administration of a mRNA COVID-19 vaccine.^{3,4} In this case report, we present two immunocompetent young adults developing herpes zoster after inactivated severe acute respiratory syndrome coronavirus (SARS-CoV-2) vaccination.

First case was a 23-year-old otherwise healthy woman who attended to our dermatology outpatient clinic with itchy and painful rash on her lower back. Her symptoms first appeared a day after she was vaccinated with inactivated SARS-CoV-2 vaccine. On examination, grouped vesicles on an erythematous base were noted. Lesions were confined in a single unilateral dermatome. She reported pain and itch which had started on the same day with rash. She was diagnosed with HZ and commenced on brivudine 125 mg tablet once daily for 7 days. Second case was a 21-year-old otherwise healthy man who presented with painful blisters at his abdomen (Figure 1). He was vaccinated with inactivated SARS-CoV-2 vaccine two days before his symptoms first appeared. On examination, painful eruption of grouped vesicles on an erythematous base in a single unilateral dermatome was observed. He was diagnosed with HZ, and valacyclovir 1 gr three times daily for seven days and analgesics were prescribed. Both patients stated that they had never experienced COVID-19-related symptoms since the beginning of pandemic, and they were well at the time of admission. After 14 days, both patients' lesions disappeared completely; moreover, they did not experience neither COVID-19-related symptoms nor postherpetic neuralgia during that period.

HZ is caused by reactivation of latent varicella zoster virus (VZV) in the sensory dorsal root ganglion. Age, stress, immunocompromised status and immunosuppressive drugs are risk factors for virus reactivation, mostly because these conditions lead to a reduction in VZV-specific T cells.⁵ COVID-19-associated HZ has been reported previously, and the median time from hospitalization to HZ beginning was found as 5,5 days in series mainly involving older adults.⁶ The mechanism of SARS-CoV-2 induced HZ is yet to be discovered, but virus's ability to deplete CD8⁺ T cells may reduce VZV-specific T cells throughout infection.⁶

This case report describes highly possible inactivated SARS-CoV-2 vaccine-related HZ in two healthy young adults. As HZ is rare in young and otherwise healthy adults, vaccine itself could be the trigger, but it is impossible to rule out reactivation of VZV by chance. Vaccines may cause immunomodulation and lead to herpes virus reactivation.⁷ Recently a case report of disseminated HZ after recombinant zoster vaccine was published, in which authors hypothesized that the immunostimulatory adjuvant in the vaccine could act as a physiologic stressor on the patient's immune system, as a consequence patient's cell-mediated immunity towards VZV fell below the threshold of containment and permitted zoster reactivation.⁸ Short delay after