

CASE REPORT

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Herpes Zoster Virus Reactivation in a 16 Year Old Female Post COVID-19 Vaccine. Case report and Review of the Literature

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ABSTRACT

Background: According to WHO, there have been 9205 fatal COVID-19 cases confirmed in Saudi Arabia out of 793,729 cases overall (5). During the development of COVID-19 vaccines, several technologies were used including DNA-based, RNA-based vaccines, non-replicating viral vector vaccines, and inactivated vaccines. **Objective:** We present a case of varicella zoster virus reactivation post COVID-19 vaccine in a young medically free 16 years old female and review of the literature using the keywords "Herpes Zoster," "varicella zoster," "shingles," "post COVID-19 vaccine", "Post COVID-19 cutaneous manifestations". **Methods:** The search was conducted in Google Scholar, Scopus, PubMed, and Web of Science data bases. **Results:** We encountered 241 published studies in regard to post COVID-19 dermatologic manifestations including post COVID-19 vaccine herpes zoster reactivation in the English literature and one case in German. Our case and 4 other reported cases in the literature are patients aged of 20 years old and below. **Conclusion:** Varicella zoster virus falls under the family of Herpesviridae, It's characterized by its ability to escape host immune system and remain dormant in ganglionic neurons. Reactivation of the infection will result in herpes zoster manifesting as painful vesicles in a dermatomal distribution. Possible link is the suppression of type-one interferons caused by the mRNA-based vaccine such as COVID-19 vaccines. Yet, potential correlation remains to be demonstrated. **Keywords:** COVID-19, COVID-19 Vaccines, Herpes Zoster, Post COVID-19 cutaneous manifestations.

1. BACKGROUND

The COVID-19 pandemic has been considered as one of the most significant health crises of this generation. Implementation of restrictive measures has shown significant efficacy to control the epidemic. Interventions included are isolation, lockdown, and contact tracing, however, vaccines are the ultimate eradication approach to COVID-19 infection. The World Health Organization (WHO) classified the illness to be caused by COVID-19 virus in 2019; it became official in February 2020 (1-3).

Worldwide, WHO has received reports of 544,324,069 COVID-19 confirmed cases, including 6,332,963 fatalities (4). According to WHO, there have been 9205 fatal COVID-19 cases confirmed in Saudi Arabia out of 793,729 cases overall (5). During the development of Covid vaccines, several technologies were used including DNA-based, RNA-based vaccines, non-replicating viral vector vaccines, and inactivated vaccines (Table 1) (6). Only four vaccines have been approved to be distributed to the public in Saudi Arabia (Pfizer/BioNTech, Oxford/AstraZeneca, Johnson & Johnson, Moderna) (7). Nevertheless, COVID-19 vaccines have been reported to cause systematic side effects like fever, fatigue, and diarrhea (6). Serious side effects were also reported like death and thrombotic complications (6, 8). In addition, cutaneous manifestations were also identified including local injection site reactions, erythromelalgia, urticaria, and morbilliform eruptions (9). One of the main post-COVID-19 vaccine skin reactions is herpes zoster virus (HZ) reactivation. VZV primary infection manifests as chicken box while secondary reactivation presents as herpes zoster (HZ). In younger, healthy adults, the incidence of herpes zoster varied from 1.2 to 3.4 per 1000 per year, while it is 3.9 to 11.8 per 1000 per year in patients over the age of 65 (10-12).

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Figure 1. Papules and vesicles lesions on an erythematous base over the lower right

2. OBJECTIVE

We present a case of a young healthy patient who is only 16 years old and has a post-COVID-19 vaccine HZ reactivation.

3. CASE REPORT

We present a 16-year-old Saudi female, medically free, who has approached our clinic at King Fahad University Hospital on 01.04.2022 complaining of severely painful grouped vesicles over her lower right trunk. The patient noticed the lesion 5 days after receiving the second dose of PfizerBioNTech vaccine on 22.03.2022 (10 days ago). First dose was taken on 02.01.2022 without any adverse effects. Pain score estimation was 9/10 on pain scale were 10 is sever none tolerated pain and 1 lowest to mild pain. There is no history of fever. Patient have a positive history of chickenpox when she was 10 years old. Otherwise, past medical history was unremarkable. Upon physical examination, as shown in Figure 1a,1b, there are papules and vesicles lesions on an erythematous base over the lower right trunk along the T10 dermatome. Biopsy was taken, as shown in Figure 2 and it was correlated with the clinical findings confirming the diagnosis of Herpes Zoster. The patient was treated with Valaciclovir 1g three times a day and gabapentin 300 mg po on first day, 300 mg po every 12 hours on the second day and 300 mg po every 8 hours on the third day. A week later, the patient was followed up with complete resolution and disappearance of active lesions. After treatment, pain score was 0/10 on pain scale.

4. DISCUSSION

Herpes zoster virus reactivation post COVID-19 vaccine has been reported in many official systems like The United States Vaccine Adverse Event Report System (VAERS) (13), Dutch pharmacovigilance centre Lareb (15), and The European Eudra Vigilance database (14)

With 2512, 300, 4103 cases of post COVID-19 vaccines HZ reactivation respectively. Further research is necessary to determine whether these figures are disproportionate. However, when paired with case reports revealing post COVID-19 Vaccine HZ reactivation, the vaccination results do point to a potential connection.

Nevertheless, there is documented reports in regard to post COVID-19 vaccine complications like post-her-

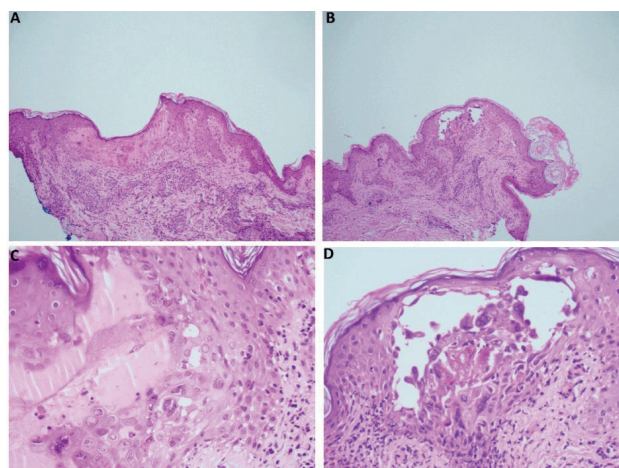


Figure 2. Hematoxylin and eosin-stained sections show intraepidermal vesicles with acantholysis (A - B). Higher magnification demonstrates keratinocytes with the classic viral cytopathic changes of herpes virus, including nuclear molding, multinucleation, and chromatin margination with nuclear "ground glass" clearing. Scattered dyskeratotic cells are also seen (C-D). (Original magnification x x 100 [A-B], x400 [C-D].

petic neuralgia (16), Meningitis, and corneal ophthalmicus (17), Additionally, the majority of the documented cases of post COVID-19 vaccine HZ reactivation is in the elderly population (18-20), patients with known comorbidities (21), patients with weakened immunity (22), and patients who smoke actively (23). However, our case is a young, medically free female who is only 16 years old. Evidence about post COVID-19 HZ reactivation in young healthy patients in the literature is scarce. As we found only 4 cases aged 20 years old and below. Table 2 (24-27) Compared the characteristics of the reported cases and ours. We noticed that 3 of the cases had mRNA-based vaccine, same as our case. While the fourth case had Adenovirus-vectored based vaccine (Astra-Zeneca). Also, three of them developed the reactivation after the Second dose, same as our case. Additionally, all reported cases have no existing skin conditions similar to ours.

Some postulated theories tried to explain the underlying mechanism of post COVID-19 vaccine HZ reactivation include:

Vaccine-induced T-cell response:

It's hypothesized that the post-COVID-19 vaccine HZ is caused by the massive T-cell mediated immune response elicited by the vaccine (28). It's plausible that the massive production of CD8+ and CD4+ T-cells has shifted naïve CD8+T cells from producing VZV-specific CD8+ T-cells. Hence, there is no effective T cells to control the dormant virus (29).

Spike hypothesis (S-protein):

It is established that mRNA-based vaccines contain Lipid nanoparticles. These particles are responsible for delivering the S-protein encoded mRNA to human cells, which are evidenced to be highly inflammatory, activating toll-like receptors, releasing different cytokines and chemokines, and exacerbating pre-existing inflammatory conditions.

Age of patient (year)	Existing comorbidities	Previous history of VZV infection (chickenpox)	Previous history of COVID-19 infection	Previous skin condition	Vaccine type	After which dose	Time of occurrence of symptoms after the vaccine:
16 (our case)	None	Yes	No	None	Pfizer- BioNTech	Second	5 days
18 (25) (herpetic keratitis)	None	No	No	None	Pfizer- BioNTech	Second	7 days
18 (26)	Only history of meningitis when 6 years old	No (received varicella vaccine)	Yes	None	Pfizer- BioNTech	Second	7 weeks
20 (27)	Asthma	No (received varicella vaccine)	No	None	Pfizer- BioNTech	Second	6 days
20 (28)	None	Not reported	No	None	AstraZeneca	First	14 days

Table 1. Characteristics of post COVID-19 vaccine herpes zoster reactivation in less than 20 years old population. (N = 4)

In addition, it's evidenced that S-protein alone is capable of inducing endothelial damage and mediates inflammatory response in human cells including, bronchial and corneal epithelial cells and microglia cells (30).

Type-1 IFN suppression: Interferon (IFN) have a central role in viral infection control, proliferation, and antibodies production. It's essential for treating various viral infections including herpes zoster due to its high potency and its ability to arrest cell cycle preventing further proliferation. Any defect in IFN signalling could impair immune response to keep the virus latent. mRNA based vaccines have shown to damage IFN-1 receptor signalling in CD8 T-cells, leading to impairment in production of effector and memory cell. This defect in signalling only happens after taking the vaccine not after acquiring the infection (31).

5. CONCLUSION

Due to the unavailability of a comparable real-time polymerase chain reaction assay, one of the primary limitations of our findings is the inability to identify the VZV strain implicated in this clinical episode. Also, one instance wouldn't be indicative of the general population due to the nature of the case report as well. We recommend developing an official reporting system for vaccines side effects in Saudi Arabia.

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- **Conflict of interest:** The authors declare that they have no conflict of interest.
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