

COVID CONCEPTS

Herpes Zoster Post-COVID-19 Vaccination in Young Adults (Under 35) Case Series

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ABSTRACT

An increasing number of reports have indicated correlation between COVID-19 vaccination and herpes zoster. While these outbreaks may be largely coincidental, the correlation warrants further investigation. Herein, we present 4 cases of herpes zoster in young healthy adults with no known risk factors for varicella virus reactivation. To date, most zoster outbreaks have been in patients above 60 years old. Thus, we believe that these cases point to a need for increased research on the topic.

INTRODUCTION

Within the last six months, there have been growing reports of herpes zoster (HZ) or shingles after vaccination with both Pfizer BNT162b2 and Moderna mRNA-1273 vaccines^{1,2,3,4,5}. HZ is caused by the varicella-zoster virus (VZV) that typically infects in childhood and remains dormant in ganglionic neurons, indefinitely. VZV is a human-specific herpesvirus that targets neurons, T lymphocytes, and epithelial cells⁶. Primary infection causes chickenpox and reactivation, later in life, causes HZ⁶. Reactivation of VZV commonly produces a characteristic painful, erythematous, vesicular rash in a dermatomal distribution⁶. The lesion is often followed by post-herpetic neuralgia, a type of neuropathic pain lasting months after rash resolution⁶. Less commonly, HZ may also lead to life-threatening conditions such as meningoencephalitis, vasculopathies, and infection⁶.

A systematic review, of all reported cases to date, demonstrated that the mean age of COVID-19-vaccine associated HZ was 62 years of age, with the majority of patients being over the age of 60⁷. In addition, HZ was reported more frequently with first dose vaccinations and with a delay of 3 to 9 days post-injection⁶. While these associations may be largely coincidental and causality remains to be demonstrated, we present four cases of HZ in healthy, young adults under the age of 35 who received either the BNT162b2 or mRNA-1273 vaccine. These cases illustrate that HZ does not only affect those over the age of 60 post-vaccination, but also those with no known risk factors. However, it is very important to emphasize that these cases do not establish association. Our goal is to call for closer investigation given the anecdotal increase in HZ cases seen in our vaccinated patients.

CASE SERIES

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Case 1. A healthy 27-year-old female with polycystic ovarian syndrome (PCOS), received her second dose of BNT162b2 vaccine in her left arm. Thirty days later, a group of itchy, painful erythematous papules and vesicles erupted on the right shoulder in the C6 dermatomal distribution (Figure 1). There was history of past varicella infection as a child, but no history of previous HZ. Seven days of valacyclovir was administered and resulted in complete resolution of lesion three weeks later.



Figure 1. Clustered, erythematous vesicles on right shoulder

Case 2. A healthy 20-year-old male with a past medical history of asthma presented with HZ six days after receiving his second injection of the BNT162b2 vaccine in his left arm. The lesion appeared in the T10 dermatomal distribution on the left abdomen (Figure 2). There was history of past varicella immunization during childhood. The patient's lesion resolved after 10 days of valacyclovir treatment.



Figure 2. Herpes zoster in T10 dermatomal distribution in 20-year-old male

Case 3. A healthy 32-year-old female with a history of nephrolithiasis presented with HZ 28 days post-vaccination with second dose of the mRNA-1273 vaccine in her left arm. The lesion was located over the right breast in a T4 dermatomal distribution. There was history of childhood infection of varicella, but no history of prior HZ. The patient's lesion resolved after 10 days of valacyclovir treatment.

Case 4. A healthy 27-year-old female with no significant past medical history presented with HZ 39 days after second dose of the mRNA-1273 vaccine in her right arm. The lesion was located on her left arm in a T1 dermatomal distribution. There was a history of childhood infection of varicella, but no history of prior HZ. The patient's lesion resolved after 10 days of valacyclovir treatment.

DISCUSSION

Our case series demonstrates a potential correlation between COVID-19 vaccination and HZ in individuals with no reactivation risk factors. In three of the presented cases, reactivation of the virus occurred about a month after injection compared to the 3-to-9-day delay previously reported⁷. Varicella reactivation presented 6 days subsequent to COVID-19 vaccination in a varicella immunized patient, indicating likely reactivation of the Oka strain varicella zoster virus (OkaVZV). In addition, all four HZ cases were associated with second dose vaccination unlike previous reports demonstrating association more frequently with first-doses⁷. These differences may indicate a different reactivation mechanism between the two groups or support mere coincidence.

The precise mechanism leading to maintenance of VZV latency and reactivation remains highly controversial and poorly understood⁶. However, it is largely believed that HZ occurs in response to a decline in cell-mediated immunity as a result of aging or immunocompromised states⁶.

BNT162b1 and mRNA-1273 vaccines direct synthesis of the SARS-COV-2 spike (S) protein, which is recognized by antigen-presenting cells and elicits a predominantly type 1 helper T (Th1) cell response^{8,9}. The mRNA-1273 vaccine was shown to elicit strong release of TNF- α , IL-2, and INF- γ in individuals aged 56 to 70 years⁷. Cytokine levels were highest after about 1-month post-injection, which would coincide with the HZ cases in three of our young adults⁷. The increase in cytokine expression and Th1 cell response may effectively disrupt immune cell homeostasis leading to VZV evasion of the innate immune system and subsequent reactivation. However, this would not be unique to the COVID-19 vaccines as HZ has also been reported after hepatitis A, influenza, rabies, and Japanese encephalitis vaccination¹⁰.

Others have hypothesized that the transient lymphopenia seen in 45.5% of individuals receiving BNT162b1 may explain HZ incidence¹¹. Apparent lymphopenia may be caused by the surge in type I interferons that regulate lymphocyte extravasation from circulation¹². Interestingly, biopsied HZ lesions are depleted of Langerhans cells that help modulate the skin's innate immunity¹³. Thus, while functionally, the immune system is intact, lymphocytes may not be able to localize to the skin and maintain VZV latency. Some other contributing factors that may explain HZ post-vaccination may include pandemic or vaccine-related emotional and physical stress, which could lead to a spike in cortisol, a known immunosuppressant.

Lastly, we must also acknowledge the variety of confounding factors in reported HZ cases during the pandemic. The pandemic and constant focus on health may have led to some patients having a lower threshold for calling their physicians leading to an increase in reported HZ cases. At the same time, other patients may have chosen to avoid healthcare spaces for fear of COVID-19 infection leading to possibly underreported HZ cases.

CONCLUSION

Taken together, these reports of HZ subsequent to BNT162b1 and mRNA-1273 vaccination warrant further studies in controlled environments to either establish coincidence or association. These future studies will be especially important in counseling patients prior to COVID-19 booster vaccines.

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