

2 Herpes zoster (Shingles) infection following COVID-19 Vaccination: An association or coincidence?

Comment [U1]:

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4
5 **Abstract:** Since early 2020, and till early 2022 the world suffered COVID-19 pandemic. Thanks to
6 medical science for developing a fast track and effective COVID-19 vaccine which is aimed to
7 reduce the infection rates and providesufficient immunity. Clinicians worldwide are monitoring
8 possible side effects and adverse events of the different COVID-19 Vaccines. In this case series,
9 we report 4 cases of Herpes Zoster infection noted in patients after having COVID-19 vaccine
10 including Pfizer, Moderna and Sinopharm Vaccines. *Discussion/Conclusion:* We present 4 pa-
11 tients who were reviewed in the outpatient clinics presenting with an erythematous, painful,
12 blistering, unilateral rash which was typical of Herpes Zoster infection following COVID-19
13 vaccination. They were between 23-54 years of age and had no significant past medical history.
14 We suspect the eruption of Herpes Zoster rash is likely linked to COVID-19 vaccination. How-
15 ever, this could also be a mere coincidence. Further research is needed to establish a proven link.

Comment [U2]: Bold

16 **Keywords:** COVID-19, vaccine, shingles, herpes zoster, adverse events

18 1. Introduction

19 As Covid 19 vaccination is rolled out in many countries, clinicians see a variety of
20 possible side effects of covid -19 vaccination in patients. In an observational study *Menni*
21 *C et al* reported systemic and local side effects following first and second doses of COVID
22 -19 vaccination. Systemic side effects included headache, fever, fatigue, chills and shivers,
23 ~~diarrhoea~~ diarrhoea, arthralgia, myalgia, and nausea. Local side effects were observed as
24 pain, swelling, tenderness, itching, swollen armpit glands, redness, and warmth. Allergic
25 reactions such as rashes, skin burning, and red welts on the face and lips were noted as
26 well. The side effects were usually mild and short-lived¹.

Comment [U3]:

27 This paper presents 4 cases where patients developed Herpes zoster within the first
28 two weeks following COVID-19 vaccination. Two of these patients had the Moderna-
29 vaccine, one had the Pfizer Vaccine, and one had the Sinopharm Vaccine. These
30 patients were aged between 23 and 54 years. Two patients had a past medical history of
31 chronic medical conditions. None of the patients had a history of prior COVID-19 infec-
32 tion or had previous Herpes zoster infection. The cases presented with a herpetic rash
33 that was erythematous, vesicular, unilateral, and painful. These patients were treated
34 with Acyclovir and analgesia. They recovered without any short-term complication

35 Varicella-zoster virus (VZV) is a human alphaherpesvirus that causes varicella
36 (chickenpox) and herpes zoster (Herpes zoster). Varicella is a common childhood illness
37 characterised by fever and vesicular skin lesions. As is characteristic of the
38 alphaherpesviruses, VZV establishes latency in the dorsal root ganglia cells. Herpes
39 zoster, caused by VZV reactivation, is a localised, painful, vesicular rash involving one or
40 a more adjacent dermatome. The incidence of herpes zoster increases with age or
41 immunosuppression. The VZV virion consists of a nucleocapsid surrounding a core that
42 contains the linear, double-stranded DNA genome; a protein tegument separates the
43 capsid from the lipid envelope, which incorporates the major viral glycoproteins. A re-
44 view study has suggested that VZV is present globally in many geographical locations
45 but is more prevalent in hot temperate climates². Herpes zoster infection occurs in 1 in 3
46 people within their lifetime. More than 10% of patients who develop Herpes zoster will

47 experience complications, including blindness, neuropathic pain, and cerebrovascular
48 events. Therefore, clinicians must be quick in recognising-recognizing the symptoms to
49 initiate treatment quickly³. Herpes zoster infections and reactivation may be subjected to
50 seasonal variations and seem more common in summer and increased exposure to
51 ultraviolet radiation⁴⁵

52 Various reports suggest vesicular skin eruptions as a presenting symptom of
53 COVID-19 infections. In many cases, the diagnosis of Herpes zoster was suggested for
54 such presentations. Different case reports support a possible coinfection of COVID-19
55 with Herpes zoster⁵⁻⁷. Indeed, in many cases, it was suggested that Herpes zoster
56 presentations raise the suspicion of mild or latent COVID-19 infection during the
57 pandemic. Shores AR reported a case of Herpes Zoster eruption associated with
58 COVID-19 infection. Shores AR mentioned several studies reporting dermatological
59 manifestations of COVID-19 infection⁷. The suppression of the immune response
60 secondary to COVID-19 infection was suggested as a possible mechanism for Herpes
61 zoster reactivation⁷.

62 To date, there are no published reports of coinfection in response to COVID-19
63 vaccination. In this case report, we present 4 cases of Herpes zoster infection within the
64 first two weeks following the COVID-19 vaccination.

65 1. Case 1:

66 A 54-year-old female patient with a history of clinically stable hypothyroidism had
67 completed the COVID-19 vaccination course. She did not have a previous history of
68 either Herpes Zoster infection or a COVID-19 disease. Nine days after the second dose of
69 COVID-19 vaccination (Pfizer), she developed a vesicular, unilateral painful rash on the
70 right side of the scalp and forehead. (figure 1 and figure 2). She had symptoms consistent
71 with a systemic illness, including fever, which was improving at the time of presentation.
72 She was treated with Oral Valacyclovir 1gram three times a day and oral analgesics. An
73 urgent referral to the Eye clinic was organised for retinal examination as the rash covered
74 the ophthalmic branch of the trigeminal nerve. Eye examination was reported as being
75 within normal limits. She recovered without any short-term complications.



76
77 **Figure 1. Herpes Zoster rash on Scalp.**

78 **Source: Photo taken with the verbal informed consent of the patient.**



79
80 **Figure 2.** Herpes Zoster rash on Forehead.

81 **Source:** Photo taken with the verbal informed consent of the patient.

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85 **Comment [U4]:** No color

86 **2. Case 2:**

87 A 23-year-old female patient had had one dose of COVID-19 vaccination (Moderna).
88 She had no past relevant medical history and was not on any medication. She did not
89 have history of COVID-19 infection. Seven days after administering the vaccine, she
90 developed a painful rash on the right side of her lower back (figure 3). This covered the
91 posterior division of Lumbar nerve distribution. The rash was vesicular, erythematous,
92 and painful. The presentation was of a typical Herpes Zoster infection. She was treated
93 with Oral Valacyclovir 1 gram three times a day, symptomatic oral analgesics, and
calamine lotion. She was followed up in the clinic after one week, and her symptoms
improved. She had not reported any subsequent complications at writing this report.



94
95 **Figure 3.** Herpes Zoster rash at Lumbar Area

96 **Source:** Photo taken with the verbal informed consent of the patient.

97
98 **Comment [U5]:** No color

3. Case 3

A 45-year-old male patient who developed a rash was clinically diagnosed as with Herpes Zoster infectionsixdays after his second dose of the COVID-19 Vaccine (Sinopharm). He had no relevant past medical history and was not on any medication. He did not report having had a COVID-19 infection in the past. He developed a painful, vesicular rash on his left arm covering the medial brachial cutaneous (T1-T2) dermatome distribution (figure 4).His rash appeared on the 6th day after the vaccination, and he presented five days after the rash appeared (day 11). The blisters had already crusted by the time of presentation,and he was treated with symptomatic analgesia only and did not require Antiviral oral medication. He did not develop short-term complications and had a complete recovery.



Figure 4. Herpes Zoster rash

Source: Photo taken with the verbal informed consent of the patient.

4. Case 4

A 38-year-old male patient with a history of Type II DM developed Herpes zoster ten days after the 1st dose of the COVID-19 vaccine (Moderna). He had no past medical history and was not on any medication.He had no previous history of either Herpes zoster or COVID-19 infections. He developed a vesicular rash covering the T6-T7 distribution on the right side of his chest. He had continued to have reasonable glycaemic control with no other complications. He was treated with Acyclovir 800mg five times a day and oral analgesics. He did not develop any short-term complications.



Figure 5. Herpes Zoster rash

Source: Photo taken with the verbal informed consent of the patient.

5. Investigations and Management.

Herpes zoster in all cases was clinically diagnosed as the presentation was of dermatological eruption of a distinct rash, which was painful, itchy vesicular/ blistering and no laboratory investigations were carried out. The rashes were typical of Herpes zoster in distribution morphology and supported by the clinical history and symptoms experienced by the patients. The cases were treated according to international clinical guidelines with Acyclovir and analgesia. Patients had a follow-up in the outpatient clinics between 1 and 2 weeks after their initial presentation. Their symptoms improved gradually, and none of them developed any short-term complications by the time of writing this report.

6. Discussion

In this case series, we have reported four known cases of Herpes zoster following the COVID-19 vaccination. The frequency of the presentations was notably higher than what we observed in our practice. Our reported case series are in the younger age group compared to the most common manifestations of Herpes zoster in those older than 50 years of age. This supports the hypothesis that these cases were associated with COVID-19 vaccination. These patients had no prior history of Herpes zoster or had a COVID-19 infection.

Different case reports have linked COVID-19 infections to Herpes zoster⁶⁻⁸, and also a case series reported Herpes zoster infection with the COVID-19 vaccination in immunocompromised patients. Furer V reported 6 patients with Autoimmune inflammatory rheumatic diseases including Rheumatoid Arthritis, Sjogren's Syndrome and undifferentiated connective tissue disease, who developed Herpes Zoster infection following COVID-19 vaccination⁹.

Theories explaining the possible association have been scarce, but the suppression of the immune response might be in play. Koshy E mentioned a system review which reported incidence for herpes zoster in North America, Europe and Asia Pacific increase to 6-8/1000 person-year at 60 years of age and 8-12/1000 person-year at 80 years of age. Kosher also mentioned a study that showed that the incidence of Herpes zoster varies from year to year. He also mentioned several studies showing higher incidence of Herpes Zoster infection in immunocompromised individuals. Patient who had bone marrow or stem cell transplant, HIV, SLE, IBD, RA, MS, Psoriatic Arthritis are at higher risk of developing Herpes Zoster infection. Cell-mediated immunity plays a role in this reactivation¹⁰.

The suppression of the immune response secondary to COVID-19 infection was suggested as a possible mechanism for Herpes zoster reactivation. COVID-19 disease is associated with damage of CD4+ T cells, rendering a patient more susceptible to developing Herpes zoster by reactivating VZV. Similarly, SARS-CoV-2 mRNA vaccines induce broad CD4+ T cell responses and may explain the response⁹.

Our observation might be due to a coincidental surge of Herpes zoster within the community. However, the hypothesis of a link between VZV reactivation and COVID-19 vaccination due to the [downregulation/down regulation](#) of the immune pathway should trigger further research, especially as the cases were in the younger patient than typically seen and the increased frequency of presentations.

Physicians should consider the diagnosis of Herpes Zoster in a recently vaccinated population presenting with typical symptoms of the eruption. We should also look at the data to consider if the Herpes zoster vaccine is indicated within a definitive or targeted population demographics, following COVID-19 Vaccination.

7. Conclusion

COVID-19 vaccination is a relatively new vaccine. Due to the urgency posed by the pandemic, unprecedented emergency steps were taken to develop COVID-19 Vaccines. After careful clinical trials and appropriate safety measures, different vaccines were launched to tackle the dire situation across the whole globe. Like any other vaccine, the COVID-19 vaccine is associated with mild side effects, including fever, soreness at the injection site, muscle pain, fatigue, and headache. While this urgency is laudable, clinicians need to be vigilant about the possible side effects of the newly launched vaccines.

So far, this case series adds to the previous evidence that suggests a link between Herpes zoster and COVID-19 vaccination. The presentations in this case series could be entirely coincidental as well. However, further studies in this respect are required to confirm or discard these findings

Institutional Review Board Statement: The study was conducted according to PHCC Research Department guidelines and has been approved by PHCC Research Subcommittee with reference number: PHCC/DCR/2021/10/060

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

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