

Varicella zoster virus reactivation following COVID-19 vaccination: a report of 3 cases

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Background: The advent of vaccination against COVID-19 brought great expectations for the control of the pandemic. As novel vaccines, much of the associated side effects were unknown. Currently, an increasing number of reports from side effects of COVID-19 vaccines have been published, namely on cutaneous reactions. These are of utmost importance to increase our knowledge about possible undesirable effects and its prevention.

Methods: We describe a series of 3 cases who presented with varicella zoster virus (VZV) reactivation following the first dose of 3 different COVID-19 vaccines.

Results: Three patients sought their Family Doctor after developing typical lesions of VZV reactivation, following a period of 3–13 days after COVID-19 vaccination. None was under immunosuppressive therapy. The 3 patients recovered in a few weeks and the subsequent doses of the vaccines were administered, without recurrence of the symptoms.

Conclusions: These cases highlight the possibility of VZV reactivation after the first dose of COVID-19 vaccines. Family Doctors should be aware of this event and play an important role informing and reassuring local communities for this possible vaccine reaction.

Key words: case report, COVID-19, SARS-CoV-2, vaccine, vaccine reaction, zoster

Background

Over the past months, we assisted to a rapid development of investigation under COVID-19 pandemic. Vaccines against COVID-19 emerged in record time and their side effects have been reported accordingly.

A recent study described the most common cutaneous reactions to the vaccines, which included delayed local reactions, local injection site reactions, urticaria, morbilliform eruptions, and erythromelalgia.¹ Varicella zoster virus (VZV) reactivation, also known as shingles, has been suggested as a cutaneous adverse reaction of COVID-19 vaccines in that study and several other reports.^{1–18}

We aimed to describe 3 cases of VZV reactivation following COVID-19 vaccination from the perspective of Family Doctors, reinforcing the possibility of this (not so) rare side effect of the vaccines.

Methods

We describe a series of 3 cases who presented with classical VZV reactivation lesions following the first dose of a vaccine for COVID-19, regarding patients' specific information, medical history, and current immunosuppressive therapy. Specifically, we also describe clinical presentation, time of appearance postvaccination, management of the disease, and outcome.

Results

Table 1 summarizes our findings. Briefly, 3 elderly patients, between 67 and 79 years old, developed mild classical symptoms

of VZV reactivation—painful rash with vesicles and crusts in the skin along 1 or 2 dermatomes—3–13 days after the first dose of 3 different COVID-19 vaccines. Patients #2 and #3 were overweight, while Patient #1 had obesity class II. Medical history included hypertension and dyslipidaemia for the 3 patients. Patient #3 had previously SARS-CoV-2 infection. None of the patients was under immunosuppressive treatment, had previous chickenpox or herpes zoster vaccination and did not recently receive any other vaccine. Patient #1 was treated with gabapentin, while Patients #2 and #3 received antiviral treatment; all patients received analgesic treatment with non-steroidal anti-inflammatory drugs (NSAIDs). Interestingly, Patient #3 had COVID-19 1 year before the vaccine, but at that time did not develop any signs of VZV reactivation. All patients completely recovered in a couple of weeks. Patients #1 and #2 received the second and the third doses of the vaccine 4 weeks after the first dose and 6 months after the second dose, respectively, without recurrence of VZV reactivation. Patient #3 received the second dose of the vaccine 6 months after the first dose, also without recurrence of the disease. The last doses of COVID-19 vaccines were administered along with seasonal influenza vaccine.

Discussion

Shingles results from VZV reactivation which is latent in the sensory root ganglia or the cranial nerves after the primary infection.¹⁹ The main risk factors involved in VZV reactivation are older age and immunosuppression caused by illness, drugs, or psychological stress.¹⁹ Here, we present a case series of shingles after COVID-19 vaccination in 3

Key Messages

We report 3 cases of varicella zoster virus (VZV) reactivation following COVID-19 vaccination with 3 different commercially available vaccines.

- Shingles' symptoms started 3–13 days after COVID-19 vaccination.
- Clinical signs did not differ from those of classical VZV reactivation.
- Management of the condition was similar to that of classical disease.
- Vaccination schedule must be completed despite this side effect.
- Additional studies are needed to clarify underlying molecular mechanisms.
- Improved clinical monitoring of COVID-19 vaccines side effects is required.

aged patients. In line with our findings, most of the VZV reactivation cases post-COVID-19 vaccination described in the literature reported patients over 50 years of age.^{2–18} Apart of advanced age, stress caused by the idea of having a new vaccine might be a risk factor for the disease.^{6,12} All the patients presented here had an increased body mass index (overweight and obesity class II), similar to other reports.¹ To our knowledge, this is not a clear risk factor for VZV reactivation. The 3 patients of our series had a medical history of hypertension and dyslipidaemia, similar to previous reports.^{1,2,4–11,13} These associated conditions may increase the risk of VZV reactivation. None of the patients was previously immunosuppressed. Though one work referred to patients under immunosuppressive therapy,³ the majority

of the patients included in other reports did not have an immunosuppressive status.^{1,2,4–18} None of the patients had previously obtained chickenpox or herpes zoster vaccines, which reduce the incidence of VZV reactivation.¹⁹ Further studies are needed to recommend these vaccines prior to COVID-19 vaccination.

Clinical presentation of VZV reactivation is very typical including rash, vesicles, and crusts, associated with neuropathic pain, with a single dermatome distribution.¹⁹ For this reason, clinical diagnosis is usually appropriate, though PCR might confirm diagnosis.¹⁹ Herein, we conclude that clinical presentation and diagnosis of VZV reactivation after COVID-19 vaccines does not vary from those of classical forms of disease, similar to previous reports.^{2–18}

Table 1. Clinical findings of 3 primary care patients with VZV reactivation following COVID-19 vaccine (2021).

Case No.	#1	#2	#3
Age	79 years	67 years	70 years
Gender	Male	Female	Female
Body mass index	36.7 kg/m ²	25.4 kg/m ²	26.9 kg/m ²
Relevant medical history	Hypertension, dyslipidaemia, gout, and benign prostatic hypertrophy	Hypertension, dyslipidaemia, diabetes mellitus type 2, chronic bronchitis, osteoporosis, and depression	Hypertension, dyslipidaemia, meningioma, and mammary carcinoma
Previous SARS-CoV-2 infection	No	No	Yes
Immunosuppressive therapy	No	No	No
Smoking history	No	No	No
Previous chickenpox or herpes zoster vaccine	No	No	No
Affected dermatome	C4–C5	T4	T9
Time after the first dose of COVID-19 vaccine	13 days	3 days	8 days
COVID-19 vaccine	Pfizer, BioNTech (BNT162b2)	Moderna (mRNA-1273)	Oxford, AstraZeneca (AZD1222 (ChAdOx1))
Treatment (oral)	Gabapentin 400 mg until 3id 8 days Acemetacin 60 mg 2id 8 days	Brivudine 125 mg id 7 days Diclofenac 75 mg 2id 5 days	Brivudine 125 mg id 7 days Ibuprofen 600 mg 2id 5 days
Second dose of COVID-19 vaccine without signs of VZV reactivation	Yes	Yes	Yes
Third dose of COVID-19 vaccine without signs of VZV reactivation	Yes	Yes	Not applicable (only 2 doses administered)
Concomitant seasonal influenza vaccination	Yes (along the third dose)	Yes (along the third dose)	Yes (along the second dose)

In our cases, VZV reactivation signs presented 3–13 days after the inoculation of the first dose of 3 different vaccines for COVID-19. Accordingly, published works point the time of presentation after 1–38 days after the first or the second dose of different commercially available vaccines.^{2–18}

VZV reactivation management includes the control of neuropathic pain and virus replication.¹⁹ Oral antiviral drugs such as Acyclovir, Valacyclovir, and Brivudine (amongst others) are effective in the cessation of virus replication and have some effect controlling the pain, if administered 72 h after the beginning of the symptoms.¹⁹ Gabapentin revealed to be effective in the control of neuropathic pain associated with VZV reactivation, as well as several classes of anti-inflammatory drugs, depending on the severity of the disease.¹⁹ In our series, Patient #1 did not comply with the therapeutic window criteria for antiviral treatment; for that reason, he approved the intake of gabapentin and a NSAID for pain control. Patients #2 and #3 were under Brivudine and NSAIDs, also with positive results. All patients completely recovered in a few weeks. In most of the cases previously reported, patients were treated with systemic antiviral agents.^{2,3,5–10,12–16} Brivudine was used in 1 report.¹⁵

As seen in Patients #1 and #3, previous reports described 10 patients who performed the second dose of the vaccine against COVID-19 without signs of VZV reactivation.^{3,8,10,13,18} Thus, shingles after the first dose of the vaccine against COVID-19 should not discourage the complete vaccination schedule.

The molecular mechanisms underlying VZV reactivation after COVID-19 vaccination remain elusive. However, we may think that an altered immune landscape involving cellular immunity might be implicated in this phenomenon,^{2–18} as established for other conditions associated with VZV reactivation.¹⁹ Interestingly, approximately 1 year before vaccination, Patient #3 was infected with SARS-CoV-2; by that time, she did not present signs of shingles. VZV reactivation has also been described synchronously with COVID-19, possibly linked to T-cell immune deregulation and stress-induced immunosuppression.²⁰ All together, these findings can provide great understanding on the immunomodulation mechanisms underlying both infection and vaccination. This topic deserves future research.

Despite the limitations of our work, namely the limited number of cases, the short interval between COVID-19 vaccine inoculation and shingles manifestation in the 3 patients here reported supports a cause–effect relation between the events, enhancing previous studies.^{1–18}

Conclusions

In conclusion, we believe that disclosing these cases through medical community is of utmost importance. Family Doctors, as first care providers, play a key role informing and reassuring local communities for this possible side effect of the vaccines against COVID-19. In addition, our work calls for more effective vigilance of COVID-19 vaccines side effects. Although sometimes disabling, VZV reactivation or shingles is a self-limited, treatable condition with good prognosis; for those reasons it should not discourage vaccination against the pandemic.

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Informed consent

Informed consent for publication of medical information was obtained from the patients.

Conflict of interest

None declared.

Data availability

The data underlying this article are available in the article.

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