

Herpes Zoster Following a Nucleoside-Modified Messenger RNA COVID-19 Vaccine

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PRACTICE POINTS

- Herpes zoster (HZ) has been reported following COVID-19 vaccination.
- Postinjection pain is common with COVID-19 vaccination, but clinical signs such as extension of pain, burning sensation, and eruption of vesicles should lead the physician to consider the diagnosis of HZ, regardless of the delay in onset between the injection and the symptoms.
- When indicated, the second vaccine dose should not be avoided in patients who are diagnosed with HZ.

Herpes zoster (HZ) was suspected as a predictive cutaneous manifestation of COVID-19, with a debated prognostic significance. We report a series of 5 cases of HZ occurring after vaccination with a nucleoside-modified messenger RNA (mRNA) COVID-19 vaccine (Comirnaty, Pfizer-BioNTech). These new cases do not prove causality between COVID-19 vaccination and HZ. The pathophysiologic mechanism remains elusive, but local vaccine-induced immunomodulation may be involved. The occurrence of HZ does not justify avoiding the second injection of vaccine due to the benefit of vaccination.

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Since the end of 2019, COVID-19 infection caused by SARS-CoV-2 has spread in a worldwide pandemic. The first cutaneous manifestations possibly linked to COVID-19 were reported in spring 2020.¹ Herpes zoster (HZ) was suspected as a predictive cutaneous manifestation of COVID-19 with a debated prognostic significance.² The end of 2020 was marked with the beginning of vaccination against COVID-19, and safety studies reported few side effects after vaccination with nucleoside-modified messenger RNA (mRNA) COVID-19 vaccines.³ Real-life use of vaccines could lead to the occurrence of potential side effects (or fortuitous medical events) that were not observed in these studies. We report a series of 5 cases of HZ occurring after vaccination with a nucleoside-modified mRNA COVID-19 vaccine extracted from a declarative cohort of cutaneous reactions in our vaccination center.

Case Series

We identified 2 men and 3 women (Table) who experienced HZ after vaccination with a nucleoside-modified mRNA COVID-19 vaccine (Comirnaty, Pfizer-BioNTech). Patients fulfilled French governmental criteria for vaccination at the time of the report—older than 75 years or a health care professional—and they were vaccinated at the vaccination center of a French university hospital. The median age of the patients was 56 years (interquartile

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The authors report no conflict of interest.

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Main Characteristics of Patients

Patient no.	Age/sex	Incriminated injection ^a	IM injection side/arm	Delay before first HZ symptom occurrence after vaccine, d	HZ side (anatomical localization)	PCR VZV	COVID-19 status before vaccination	History of HZ
1	51/F	First	Left	1	Left (superior limb)	Positive	Resolutive infection February 2020	No
2	56/M	Second	Left	24	Left (chest)	Not done	Never infected	Yes
3	82/M	First	Left	6	Right (superior limb)	Positive	Never infected	No
4	64/F	First	Left	15	Left (inferior limb)	Not done	Never infected	No
5	53/F	First	Left	1	Left (inferior limb)	Not done	Never infected	No

Abbreviations: F, female; HZ, herpes zoster; IM, intramuscular; M, male; PCR, polymerase chain reaction; VZV, varicella-zoster virus.

^aIdentified as first or second.

range [IQR], 51–82 years). One patient was diagnosed with COVID-19 in February 2020. A medical history of HZ was found in 1 patient. No medical history of immunosuppression was noted. Herpes zoster was observed on the same side of the body as the vaccination site in 4 patients. The median delay before the onset of symptoms was 6 days (IQR, 1–15 days) after injection. The median duration of the symptoms was 13 days (IQR, 11.5–16.5 days). Clinical signs of HZ were mild with few vesicles in 4 patients, and we observed a notably long delay between the onset of pain and the eruption of vesicles in 2 cases (4 and 10 days, respectively). The clinical diagnosis of HZ was confirmed by a dermatologist for all patients (Figures 1 and 2). Polymerase chain reaction assays for the detection of the varicella-zoster virus were performed in 2 cases and were positive. A complete blood cell count was performed in 1 patient, and we observed isolated lymphopenia (500/mm³ [reference range, 1000–4000/mm³]). Herpes zoster occurred after the first dose of vaccine in 4 patients and after the second dose for 1 patient. Three patients were treated with antiviral therapy (acyclovir) for 7 days. Three patients recovered from symptoms within 2 weeks and 2 patients within 1 week.

Comment

We report a series of HZ cases occurring after vaccination with a nucleoside-modified mRNA COVID-19 vaccine. We did not observe complicated HZ, and most of the time, HZ lesions were located on the same side of the body as the vaccine injection. One case of HZ after COVID-19

vaccination was reported by Bostan and Yalici-Armagan,⁴ but it followed injection with an inactivated vaccine, which is different from our series. Herpes zoster remains rarely reported, mainly following mRNA COVID-19 vaccination.⁵

Cases of HZ after vaccination have been reported after the live attenuated zoster or yellow fever vaccines, but HZ should not appear as a concomitant effect after any type of vaccines.^{6,7} Kawai et al⁸ reported that the incidence rate of HZ ranged from 3 to 5 cases per 1000 person-years in North America, Europe, and Asia-Pacific. The risk for recurrence of HZ ranged from 1% to 6% depending on the type of study design, age distribution of studied populations, and definition.⁸ In another retrospective database analysis in Israel, the incidence density rate of HZ was 3.46 cases per 1000 person-years in the total population and 12.8 cases per 1000 person-years in immunocompromised patients, therefore the immunocompromised status is important to consider.⁹

In our declarative cohort of skin eruptions before vaccination, we recorded 11 cases of HZ among 148 skin eruptions (7.43%) at the time of the study, but the design of the study did not allow us to estimate the exact incidence of HZ in the global COVID-19–vaccinated population because our study was not based on a systematic and prospective analysis of all vaccinated patients. The comparison between the prevalence of HZ in the COVID-19–vaccinated population and the nonvaccinated population is difficult owing to the lack of data about HZ in the nonvaccinated population at the time of our analysis. Furthermore, we did not include all vaccinated patients in a prospective follow-up. We highlight the



FIGURE 1. Herpes zoster with localized, fluid-filled vesicles on the internal and posterior aspects of the right arm in a patient who received a nucleoside-modified messenger RNA COVID-19 vaccine (patient 3).



FIGURE 2. Scattered discrete vesicles on the anterior aspect of the left elbow and forearm with predominant painful symptoms and positive polymerase chain reaction assay for detection of varicella-zoster virus in a patient who received a nucleoside-modified messenger RNA COVID-19 vaccine (patient 1).

importance of medical history of patients that differed between vaccinated patients (at the time of our analysis) and the global population due to French governmental access criteria to vaccination. The link to prior SARS-CoV-2 infection was uncertain because a medical history of COVID-19 was found in only 1 patient. Only 1 patient had a history of HZ, which is not a contraindication of COVID-19 vaccination.

Postinjection pains are frequent with COVID-19 vaccines, but clinical signs such as extension of pain, burning sensation, and eruption of vesicles should lead the physician to consider the diagnosis of HZ, regardless of the delay between the injection and the symptoms. Indeed, the onset of symptoms could be late, and the clinical presentation initially may be mistaken for an injection-site reaction, which is a frequent known side effect of vaccines. These new cases do not prove causality between COVID-19 vaccination and HZ. Varicella-zoster virus remains latent in dorsal-root or ganglia after primary infection, and HZ caused by reactivation of varicella-zoster virus may occur spontaneously or be triggered. In our series, we did not observe medical history of immunosuppression, and no other known risk factors of HZ (eg, radiation therapy, physical trauma, fever after vaccination) were recorded. The pathophysiologic mechanism remains elusive, but local vaccine-induced immunomodulation or an inflammatory state may be involved.

Conclusion

Our case series highlights that clinicians must remain vigilant to diagnose HZ early to prevent potential complications, such as postherpetic neuralgia. Also, vaccination should not be contraindicated in patients with medical history of HZ; the occurrence of HZ does not justify avoiding the second injection of the vaccine due to the benefit of vaccination.

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