Conflict of interest

All the authors declare no conflict of interest.

Funding sources

There are no founding sources.

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DOI: 10.1111/jdv.17645

Varicella-zoster and herpes simplex virus reactivation post-COVID-19 vaccination: a review of 40 cases in an International Dermatology Registry

Editor,

Since December 2020, the American Academy of Dermatology and the International League of Dermatologic Societies' COVID-19 Dermatology Registry has tracked dermatologic reactions post-COVID-19 vaccination. Within months, a variety of cutaneous manifestations were reported after the Moderna and Pfizer-BioNTech COVID-19 vaccines.[1] As of April 2021, a total of 672 possible vaccine-related skin reactions have been reported by healthcare providers. Here, we evaluate the first 40 cases of varicella-zoster virus (VZV) and herpes simplex virus (HSV) reported in the registry after COVID-19 vaccination with either the Moderna or the Pfizer-BioNTech vaccines.

Of 40 cases of herpesvirus activation diagnosed by healthcare providers after vaccination, 35 cases were VZV reactivation and 5 cases were HSV reactivation (Table 1). The median age of patients was 46 (IQR 36–67). The majority were female (70%), white (80%), and from the United States (95%).

Among the 35 patients with VZV reactivation (Fig. 1), 19 received Pfizer-BioNTech and 16 received Moderna. Most (77%) cases occurred after the first vaccine dose only, and none of the patients had repeat viral flares after both doses. Median onset was 7 days (IQR 2–13) from vaccination to the first VZV symptom, and symptoms lasted median of 7 days (IQR 5–12). Patients were primarily treated with valacyclovir/acyclovir (86%). One patient was not planning on receiving their second vaccine dose due to VZV after the first dose. Data on prior VZV vaccination were available for 14 individuals, and of these, only one had received a VZV vaccine (live-attenuated), 7 years prior.

Of 5 patients reported with HSV reactivation post-COVID vaccine, 4 received Pfizer-BioNTech and 1 received Moderna. Four of these cases occurred after the first dose, and one case occurred only after the second dose. Median onset of first HSV symptom was 13 days (IQR 8–15) post-vaccination and lasted median of 7 days (IQR 3–7). Four patients (80%) received valacyclovir/acyclovir as treatment, and none delayed their second vaccine dose.

One limitation is that the registry did not routinely ascertain whether VZV/HSV was diagnosed by the reporter based on laboratory testing (e.g. PCR) or on clinical grounds alone, although clinical diagnosis of zoster without laboratory testing has a reported positive predictive value of 86%–92%.[2,3] Additional limitations are incomplete VZV vaccination history and immune status data, which hinder the ability to draw conclusions about the relationship between prior vaccination, immunocompromised status, and risk of VZV reactivation post-COVID vaccination. Furthermore, an epiphenomenon cannot be ruled out since the registry is not designed to establish the incidence of zoster in the vaccinated group or compare it to the incidence in a non-vaccinated group.

VZV reactivation after COVID vaccination has been reported in case reports and small case series,[4–7] and it has also been reported after other vaccines, including yellow fever, hepatitis A, rabies and influenza.[8] While other cutaneous vaccine reactions reported to the registry occurred primarily after Moderna, such as delayed large local reactions,[9] VZV reactivation events occurred after both Moderna and Pfizer in similar proportions in this study, suggesting that reactivation may be the result of an immune reaction process to mRNA vaccines in general. Although the precise

Table 1 Characteristics of 40 HSV and VZV Reactivation Events Reported after Moderna or Pfizer-BioNTech COVID-19 vaccination

	VZV reactivation Unique reports *N* (%) (*n* = 35)	HSV reactivation Unique reports *N* (%) (*n* = 5)	Total Unique reports *N* (%) (*n* = 40)
COVID-19 vaccine type			
Moderna	16 (46)	1 (20)	17 (42)
Pfizer	19 (54)	4 (80)	23 (58)
Reporter title			
Dermatologist	25 (71)	5 (100)	30 (75)
Other physician	9 (26)	0 (0)	9 (23)
Nurse practitioner	1 (2.9)	0 (0)	1 (2.5)
Patient age (Median, IQR)	46 (35–68)	39 (36–53)	46 (36–67)
Patient sex (Female)	24 (69)	4 (80)	28 (70)
Patient race/ethnicity			
White	28 (80)	4 (80)	32 (80)
Asian	2 (5.7)	0	2 (5.0)
Black/African American	2 (5.7)	0	2 (5.0)
Hispanic/Latino	2 (5.7)	1 (20)	3 (7.5)
Unknown	1 (2.9)	0 (0)	1 (2.5)
Patient Country			
United States	34 (97)	4 (80)	38 (95)
Canada	0	1 (20)	1 (2.5)
Saudi Arabia	1 (2.7)	0	1 (2.5)
Prior SARS-CoV-2 infection			
No	34 (97)	5 (100)	39 (98)
SARS-CoV-2 PCR+	1 (2.7)	0 (0)	1 (2.5)
Vaccine dose number associated with reaction			
First	27 (77)	4 (80)	31 (78)
Second	8 (23)	1 (20)	9 (23)
Both	0 (0)	0 (0)	0 (0)
Rash location[†]			
Face	3 (8.6)	4 (80)	7 (18)
Head	4 (11)	0 (0)	4 (10)
Neck	2 (5.7)	0 (0)	2 (5.0)
Vaccinated arm	3 (8.6)	0 (0)	3 (7.5)
Non-vaccinated arm	1 (2.9)	0 (0)	1 (2.5)
Chest	14 (40)	0 (0)	14 (35)
Abdomen	10 (29)	0 (0)	10 (25)
Back	16 46)	0 (0)	16 (40)
Buttocks	3 (8.6)	0 (0)	3 (7.5)
Leg	3 (8.6)	0 (0)	3 (7.5)
Oral mucosa	0 (0)	1 (20)	1 (2.5)
Vaccine allergy history			
None	35 (100)	5 (100)	40 (100)
Past medical history			
None	14 (40)	4 (80)	18 (45)
Hypertension	7 (20)	1 (20)	8 (20)
Rheumatologic disease	3 (8.6)	0 (0)	3 (7.5)
Morbid obesity	2 (5.7)	0 (0)	2 (5.0)
Diabetes mellitus	2 (5.7)	0 (0)	2 (5.0)
Cardiovascular disease	1 (2.9)	0 (0)	1 (2.5)
Obstructive lung disease	1 (2.9)	0 (0)	1 (2.5)
Chronic renal insufficiency	1 (2.9)		1 (2.5)

Table 1 *Continued*

	VZV reactivation Unique reports *N* (%) (*n* = 35)	HSV reactivation Unique reports *N* (%) (*n* = 5)	Total Unique reports *N* (%) (*n* = 40)
Liver disease	1 (2.9)	0 (0)	1 (2.5)
Immunodeficiency	1 (2.9)	0 (0)	1 (2.5)
Other	8 (23)	0 (0)	8 (20)
Treatment			
Valacyclovir/Acyclovir	30 (86)	4 (80)	34 (85)
Topical steroids	1 (2.9)	0 (0)	1 (2.5)
Acetaminophen	2 (5.7)	0 (0)	2 (5.0)
Gabapentin	4 (11)	0 (0)	4 (10)
None	3 (8.6)	1 (20)	4 (10)

†Providers were able to check off multiple rash locations for each patient.

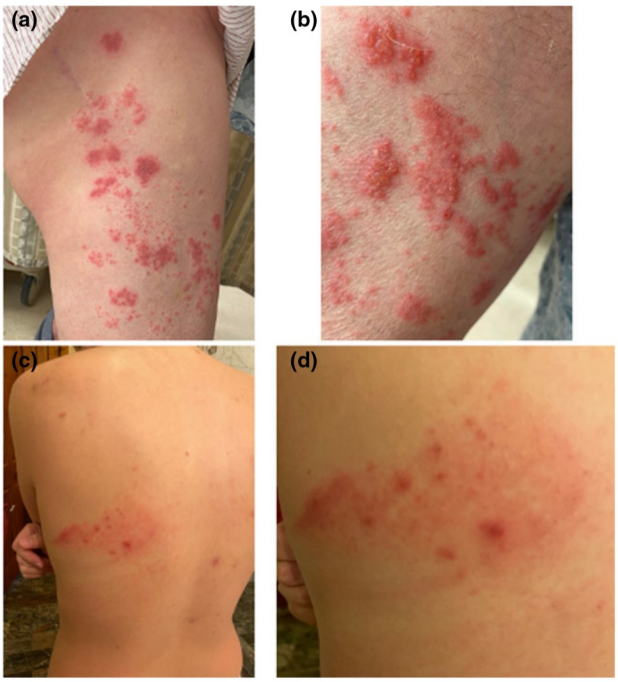

Figure 1 Representative images of Varicella-Zoster Virus reactivation following COVID-19 vaccination. (a) Zoster flare on leg of a patient 14 days after the second dose of Pfizer COVID-19 vaccination (b) same patient, close-up view of vesicles. (c) Zoster flare on the back of a patient 18 days after the first dose of Pfizer COVID-19 vaccination (d) same patient, close-up view of dermatome.

mechanism is not known, herpesvirus reactivation may occur due to innate- or cell-mediated immune defense failures initiated by the host response to vaccination. VZV reactivation has also been reported following SARS-CoV-2 infection itself, and a similar immunosuppressive mechanism has been suggested.[10]

Overall, COVID-19 vaccination is still recommended, as the benefits of COVID-19 vaccination vastly outweigh the potential risk of herpesvirus reactivation. Further research is needed to elucidate the risk factors for and mechanisms underlying this process. We advise healthcare workers to be aware of this potential consequence and to begin appropriate treatment when reactivation is suspected.

Acknowledgements

The authors would like to thank Dr. Stephanie Florez-Pollack for contributing clinical photographs for this work, as well as healthcare providers worldwide for entering their data in the AAD/ILDS COVID-19 Dermatology registry. The patients in this manuscript have given written informed consent to the publication of their photographs.

Conflicts of interest

Drs. Freeman, Hruza, Rosenbach, Lipoff and Fox are part of the American Academy of Dermatology (AAD) COVID-19 Ad Hoc Task Force. Dr. French is the President, and Dr. Lim is board member of the ILDS. Dr. Thiers is the outgoing President of the AAD. Dr. Freeman is an author of COVID-19 dermatology for UpToDate. Dr. Freeman receives grant support from the ILDS for the COVID-19 Dermatology Registry. Dr. Freeman is a co-author for UpToDate on COVID-19 Dermatology.

Funding sources

International League of Dermatological Societies provided grant support to Massachusetts General Hospital for the administration and maintenance of the Dermatology COVID-19 registry. The American Academy of Dermatology provided in-kind administrative support.

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DOI: 10.1111/jdv.17646

Two cases of pityriasis rosea after the injection of coronavirus disease 2019 vaccine

To the editor,

The incidence of cutaneous manifestation in coronavirus disease 2019 (COVID-19) patients was around 20%.[1] Among the reported cutaneous reactions after the inoculation of COVID-19 vaccination till now, the most common reactions were delayed large local reactions, local injection site reactions, urticaria and morbilliform eruptions.[2] Pityriasis rosea (PR) was found to be one of the rare cutaneous symptoms caused by the COVID-19 vaccination.[2] Here, we report 2 cases of PR after the COVID-19 vaccination.

The first case was one 19-year-old man who came to the department of dermatology for 1-month history of pruritus papulosquamous lesion. His lesion appeared 2 days after the first dose injection of COVID-19 vaccine. This inactivated vaccine was produced by the Beijing Institute of Biological Products Company. His colleagues who had injected the same batch of vaccine had no similar symptoms till now. On physical examination, he had several oval pink-to-brown-coloured thin scaly plaques on the trunk and proximal extremities (Fig. 1a–c). Blood routine was normal. Besides, he completed 3 times of PCR test for COVID-19, and the latest test occurred the day before the visit. All negative results of the nucleic test indicated no infection of COVID-19. He was diagnosed with PR according to the classical clinical feature. After 1-week treatment of valaciclovir 300mg bid orally and mometasone furoate to inhibit itch when needed, the patient's manifestation had obvious improvement. He did not get the second dose of vaccination due to the eruption of PR after the first dose inoculation.

The second case was a 51-year-old man. He got the vaccination from the same company as the first patient as mentioned above. He developed itchy fusiform patches in the trunk 7 days after the second dose injection of COVID-19 vaccine and came to our department 3 days after the onset of the cutaneous symptom. He claimed slight similar lesions several days after the first dose inoculation without detailed picture. He reported no preceding disorder, no systemic discomfort, no cutaneous contacts or no new drug exposures. Physical examination indicated annular and oval lesion covering by thin scales across the neck, trunk, bilateral groins and proximal extremities, in a 'Christmas tree' pattern (Fig. 1d,e). During the process, the patient had no fever, cough or any other symptoms. Based on the diagnosis of PR, we treated him with ganciclovir 250 mg bid orally and got the improvement.

PR is a self-limited papulosquamous disorder associated with virus infection. Previous study reported the onset of PR several