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LETTERS TO THE EDITOR

Potential risk factors for Varicella-zoster virus reactivation after COVID-19 vaccination

To the Editor,

During this Sars-CoV-2 era, several different vaccines have been developed to counter the spreading of the virus, and more and more attention has been paid to the adverse effects related to their administration. The most common described cutaneous side effects are delayed large local reactions, local injection site reactions, urticarial eruptions, and morbilliform eruptions.[1] Recently, there have been several reports of a potential association between the injection of COVID-19 vaccines (both the mRNA and the inactivated ones) and the reactivation of Varicella-zoster virus (VZV). Reactivation of this virus leads to a painful rash commonly known as shingles.

Rodríguez-Jiménez et al. recently published a series of 5 cases of VZV reactivation after SARS-CoV-2 BNT162b2 mRNA vaccination.[2] Lladó et al. made a first review of the cases reported in literature[3]; here, we want to make an update and find any potential clue to value the risk of VZV reactivation after COVID-19 vaccination.

We analyzed 93 cases of VZV reactivation following the COVID-19 vaccine reported in literature.[1,2,4–36] We decided to focus only on cases with enough information to allow for a correct risk assessment, for example, we did not include all the reports where age or sex were not present. There was no significant difference between males and females (44 men vs 49 women), and, in accordance with the previous observations,[3] the majority of the VZV reactivations were secondary to mRNA vaccines (46 following Pfizer's BNT162b2 and 19 following Moderna's mRNA-1273 vs 18 following Astrazeneca's AZD1222 (ChAdOx1), 2 following Johnson & Johnson's JNJ-78436735 (Ad26.COV2.S), 1 following Bharat Biotech's BBV152 (Covaxin), 1 following Sinopharm's BBIBP-CorV vaccine (Vero Cells), and 1 following Sputnik V (Gam-COVID-Vac); 5 not specified). Most of the cases developed after the injection of the first dose of the vaccine rather than the second one (67 vs 21; 5 not specified) with a high variability regarding time to the onset after injection (average 8.6 ± 7.2 days, from one to 38 days). The average age was 57.8 ± 17.3 years. The majority of patients were treated with standard antiviral therapy (Acyclovir or Valacyclovir). Relevant variables are reported in Table 1.

As a possible explanation for the VZV reactivation, we support the hypothesis of an immunomodulation mechanism triggered by the vaccination with a consequent failure to maintain the virus controlled.[3] For example, some authors suggested a temporary inability of the VZV-specific $CD81^+$ cells to control the virus, due to a shifting of naive CD81 cells.[4]

According to these data, the risk of developing VZV reactivation after COVID-19 vaccination seems to be higher in patients who received mRNA vaccines, those who received the first dose rather than the second one and, to a lesser extent, those in the fifth or sixth decades of life. We know that the relationship between VZV reactivation and COVID-19 vaccination could be coincidental and, in this particular historical moment, vaccination remains the priority, as it represents our fundamental weapon against the pandemic; however, we think it is important to report this possible association to

TABLE 1 Main features of the 93 cases analyzed

Sex	
Female	49
Male	44
Mean age	57.8
Age range	21–94
Vaccine type	
BNT162b2 (Pfizer)	46
mRNA–1273 (Moderna)	19
AZD1222 (AstraZeneca)	18
JNJ–78436735 (Johnson & Johnson's)	2
BBV152 (Bharat Biotech)	1
BBIBP-CorV (Sinopharm)	1
Gam-COVID-Vac	1
Not specified	5
Dose	
First	67
Second	21
Not specified	5
Time to VZV reactivation	
Mean	8.6
Minimum	1
Maximum	38

the scientific community, as more and more evidence is emerging. In fact, identifying patients at risk would allow early antiviral therapy to be initiated and a better clinical course to be achieved.

KEYWORDS

COVID-19 vaccine, herpes zoster reactivation, Varicella-zoster virus

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None.

CONFLICTS OF INTEREST

None declared.

ETHICAL APPROVAL

The authors confirm that the ethical policies of the journal, as noted on the journal's author guidelines page, have been adhered to. No ethical approval was required as this is a review article with no original research data.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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