NOTES & COMMENTS

Varicella zoster virus reactivation and mRNA vaccines as a trigger

To the Editor: We read with great interest the report by Channa et al,[1] "Herpes zoster reactivation after mRNA-1273 (Moderna) SARS-CoV-2 vaccination." Currently, vaccination against SARS-CoV-2 is being carried out worldwide. As a consequence, a wide variety of cutaneous adverse effects after COVID-19 vaccination are being described.[2] Over the course of the last months, a fair number of herpes zoster cases developing after the administration of COVID-19 vaccines have been reported.[1-5]

Varicella zoster virus (VZV) reactivation is triggered mainly by impaired cell-mediated immunity, whether it be age-related, disease-related, or iatrogenic. Vaccines are not a common trigger for VZV reactivation, and with the exception of VZV reactivation following the VZV vaccine, few cases have been reported. Rodriguez-Jiménez et al[5] reported 3 cases of herpes zoster following vaccination against hepatitis A, rabies, and influenza, respectively.

To our knowledge, 52 cases of VZV reactivation following the COVID-19 vaccine have been reported to date. Interestingly, only 1 of 52 cases, was secondary to an inactivated vaccine, whereas the rest of them were secondary to mRNA vaccines (ie, Pfizer's BNT162b2 and Moderna's mRNA-1273)[1] (Table I). The majority of the cases developed after the first dose versus the second dose of the vaccine (35 vs 15, respectively; 2 unknown), and there was no significant sex predominance (22 women vs 20 men; 10 not specified). However, it must be taken into account that some of the series may suffer from a selection bias.

Surprisingly, most of the patients were middle-aged (ie, in their fifth to sixth decades of life), as someone would expect to observe the highest incidence rates among the oldest patients. Time to the onset of symptoms was highly variable, ranging from 1 to 26 days and showing a median of 6 days. The difference in the time of onset having received the first or the second vaccine dose was not consistent between the series. Lastly, the sample distribution was, overall, highly heterogeneous in terms of comorbidities, past history of herpes zoster, and previous VZV vaccination.

VZV reactivation in patients infected with SARS-CoV-2 has been described. The suggested pathogenic mechanism was induced lymphopenia and the functional impairment of lymphocytes, particularly $CD8^+$ T cells and natural killer cells. With regard to COVID-19 vaccines, it is postulated that, as a product of a massive shifting of naïve $CD8^+$ cells, VZV-specific $CD8^+$ cells are not temporarily capable of controlling VZV.[4] The question of why VZV reactivation occurs almost exclusively with mRNA-based COVID-19 vaccines and not with viral vector or inactivated COVID-19 vaccines remains to be answered. We are aware that the relationship between COVID-19 vaccination, particularly with

Table I. Reported cases of VZV reactivation after COVID-19 mRNA vaccination

Authors	n	Vaccine type	First dose	Second dose	Time to onset (days)[range (median)]	Age (years) [range (median)]	Sex
Lee et al[2]	20	mRNA-1273 (n = 14) and BNT162b2 (n = 6)	15	5	2-26 (6.9)	37-77 (56)	10 M, 10 F
McMahon et al[3]	10	mRNA-1273 (n = 5) and BNT162b2 (n = 5)	6	4	NS	NS	NS
Psichogion et al[4]	7	BNT162b2	5	2	7-20 (9)	51-94 (77)	4 M, 3 F
Rodriguez-Jiménez et al[5]	5	BNT162b2	3	2	1-16 (5.4)	39-58 (48)	2 M, 3 F
Others[2-5]	9	mRNA (not specified), mRNA-1273, and BNT162b2	7	1	2-14 (5)	36-81 (49)	3 M, 6 F

F, Female; *M*, male; *NS*, not specified.

mRNA-based vaccines, and VZV reactivation could be coincidental. Nonetheless, as new evidence continues to emerge, it becomes harder to deny. In our opinion, clinicians should be aware of this possible adverse effect of mRNA vaccines.

Iñigo Lladó, MD, Alberto Fernández-Bernáldez, MD, and Pedro Rodríguez-Jiménez, MD, PhD

From the Department of Dermatology, Instituto de Investigación Sanitaria la Princesa, Hospital Universitario de La Princesa, Madrid, Spain.

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Correspondence to: Pedro Rodríguez-Jiménez, MD, PhD, Department of Dermatology, Instituto de Investigación Sanitaria la Princesa, Hospital Universitario de La Princesa, Diego de León Street 62, CP 28006, Madrid, Spain

E-mail: pedro.rodriguez.jimenez90@gmail.com

Conflicts of interest

None disclosed.

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