Disseminated and localised herpes zoster following Oxford-AstraZeneca COVID-19 vaccination

Sir,

Since the emergence of the coronavirus disease 2019 pandemic, vaccination has become crucial to avoid severe complications and achieve herd immunity.[1] Two variants of coronavirus disease 2019 vaccine have been approved by the European Medicines Agency: one containing a nucleoside-modified messenger RNA that encodes the viral spike glycoprotein of severe acute respiratory syndrome coronavirus 2, while the other is a viral vector coronavirus disease 2019 vaccine encoding the severe acute respiratory syndrome coronavirus 2 S glycoprotein.[2]

Herpes zoster, caused by reactivation of the latent varicella-zoster virus, is attributed to depressed cell-mediated immunity. This condition frequently affects the elderly due to adaptive immunosenescence.[1,3] Known risk-factors include immunosuppressive disease and treatment, which suppress the cell-mediated immunity. Recent reports suggest occurrence of herpes zoster in immunocompetent individuals without risk-factors, following the Pfizer (BNT162b2), Moderna (mRNA-1273), Covaxin (BBV152), and AstraZeneca (AZD1222) vaccines against coronavirus disease 2019 [Table 1].[4-9]

Here, we report three cases of herpes zoster following vaccination with the Oxford-AstraZeneca coronavirus disease 2019 vaccine, and discuss possible patho-mechanisms [Table 2].

A 79-year-old male presented with painful, vesicular eruptions on his left arm and hand, distributed along the C7, C8, and T1 dermatomes. He had received the first-dose of Oxford-AstraZeneca coronavirus disease 2019 vaccine on the same arm four days before [Figure 1a]. Subsequently, the vesicular eruptions involved his face, chest, back, and extremities over the next three days, and fever was an associated symptom [Figures 1b and 1c]. A systemic review was negative. The patient provided history of varicella without previous herpes zoster episode. He was receiving oral prednisolone (5mg/day) and antihistamines for last one week, along with pramipexole and levodopa for concomitant adult-onset atopic dermatitis and parkinsonism respectively. His baseline blood examination revealed lymphopenia (798 cells/mm^3), and the count reduced to 569 cells/mm^3 after one-week prednisolone treatment. Serum creatinine, alanine aminotransferase and chest X-ray were normal. Reverse transcription polymerase chain reaction testing for coronavirus disease 2019 was negative. Tzanck smear demonstrated multinucleated giant cells. Serum varicella-zoster virus immunoglobulin G was positive, while immunoglobulin M was negative. We administered intravenous acyclovir 800 mg every 8 h for disseminated herpes zoster. Over the next two days, pustules developed, and pus culture yielded staphylococcus aureus sensitive to amoxycillin. The rash resolved and his clinical condition improved after continuing intravenous acyclovir and amoxycillin/clavulanic acid 1.2 g every 8 h for one week.

The other two cases developed their first episode of localised herpes zoster, ipsilateral to the site of vaccination. One was a 91-year-old male who developed left arm swelling three days post first dose of the Oxford-AstraZeneca vaccine. Subsequently, painful vesicular eruptions developed over his left arm (C7-8 dermatome). He had a history of stage three chronic kidney disease. The other patient was a 25-year-old female who presented with painful vesicular eruptions over her left neck and shoulder (C3-C4 dermatome) one week after receiving her first dose of the Oxford-AstraZeneca vaccine. There was no history of systemic disease, immunosuppressive condition, recent infection, or stress. A seven-day course of oral famciclovir resolved the lesions in both patients. Neither patient had received the second dose of the Oxford-AstraZeneca vaccine during our follow-up.

Varicella-zoster virus reactivation is reported in 15% and 50% of immunocompetent and immunocompromised patients respectively.[10] Disseminated herpes zoster indicates more than twenty skin eruptions outside the primary or adjacent dermatomes.[11] It was perceived that immunosuppression is the only risk-factor for disseminated herpes zoster, however, Bollea-Garlatti *et al*. suggested advanced age to be an independent risk-factor due to adaptive immunosenescence.[10] Post-vaccination herpes zoster has been reported following

How to cite this article: Jiang ZH, Wong LS, Lee CH, Hsu TJ, Yu YH. Disseminated and localised herpes zoster following Oxford-AstraZeneca COVID-19 vaccination. Indian J Dermatol Venereol Leprol 2022;88:445.

Received: August, 2021 **Accepted:** October, 2021 **EPub Ahead of Print:** April, 2022 **Published:** April, 2022

DOI: 10.25259/IJDVL_819_2021 **PMID:** 35389012

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Table 1: Reported cases of varicella-zoster virus reactivation after coronavirus disease 2019 vaccination

Case series	Vaccine type	Number of patients	1st dose	2nd dose	Gender	Age	Type of herpes zoster	Immune status of patients
Arora *et al*. 2021	Covaxin (BBV152)	1	1	0	Male: 1	Above 60 years old: 1 Below 60 years old: 0	Localized	Diabetes mellitus: 1
Chiu *et al*. 2021	Moderna (mRNA-1273)	1	1	0	Male: 1	Above 60 years old: 1 Below 60 years old: 0	Localized	Not specified
	Oxford-AstraZeneca (AZD1222)	2	2	0	Male: 2	Above 60 years old: 0 Below 60 years old: 2	Localized	Not specified
Lee *et al*. 2021	Moderna (mRNA-1273)	14	12	2	Male: 5 Female: 9	Above 60 years old: 7 Below 60 years old: 7	Localized	Diabetes mellitus: 1 Crohn's Disease: 1 Polycythemia Vera treated with ruxolitinib: 1
	Pfizer-BioNTech (BNT162b2)	6	3	3	Male: 5 Female: 1	Above 60 years old: 2 Below 60 years old: 4	Localized	Heart failure: 1 Kidney failure: 1
Psichogiou *et al*. 2021	Pfizer-BioNTech (BNT162b2)	7	5	2	Male: 4 Female: 3	Above 60 years old: 5 Below 60 years old: 2	Localized	Prostate cancer: 1 Heart failure: 1
Fathy *et al*. 2021	Pfizer-BioNTech (BNT162b2)	19	27	8	Male: 11 Female: 24	Not specified Median age: 46	Localized	Diabetes mellitus: 2 Morbid obesity: 2 Immunodeficiency: 1
	Moderna (mRNA-1273)	16						
Rodríguez-Jiménez *et al*. 2021	Pfizer-BioNTech (BNT162b2)	5	3	2	Male: 2 Female: 3	Above 60 years old: 0 Below 60 years old: 5	Localized	Not specified
Furer *et al*. 2021	Pfizer-BioNTech (BNT162b2)	6	5	1	Male: 0 Female: 6	Above 60 years old: 1 Below 60 years old: 5	Localized	Rheumatic arthritis under immunosuppressant: 4 Sjogren's syndrome under hydroxychloroquine: 1 Anti-phospholipid antibody syndrome: 1

Table 2: Demographic data of patients in our series who developed herpes zoster following Oxford-AstraZeneca coronavirus disease 2019 vaccination

Patient's data	Case 1	Case 2	Case 3
Age	79	91	25
Gender	Male	Male	Female
Comorbidities	Late-onset atopic dermatitis Parkinsonism	Chronic kidney disease, stage 3	No
Medications	Prednisolone 5 mg/day for 1 week pramipexole and levodopa	No	No
Time interval between vaccination and onset of herpes zoster	4 days after the first dose	3 days after the first dose	7 days after the first dose
Dermatome	C7, C8 and T1, then disseminated	C7-8 dermatome	C3-C4 dermatome
Other symptoms	Fever, malaise	No	No
Treatment for herpes zoster	Intravenous acyclovir 800 mg Q8H for 1 week	Oral famciclovir 500 mg Q12H for 1 week	Oral famciclovir 500 mg Q8H for 1 week
Previous vaccination for varicella-zoster virus	No	No	No
History of previous herpes zoster	No	No	No
Polymerase chain reaction test of severe acute respiratory syndrome coronavirus 2	Negative	Negative	Negative

inactivated influenza, hepatitis A, rabies, and Japanese encephalitis vaccines.[12] Recently, varicella-zoster virus reactivation following severe acute respiratory syndrome coronavirus 2 BNT162b2 mRNA vaccination has been reported, but the mechanism is unclear. Two of our cases were elderly and susceptible to varicella-zoster virus reactivation. The case with disseminated herpes zoster received prednisolone 5 mg/day for one week to control a flare up of atopic dermatitis. Notably, short-term systemic corticosteroid use is not considered a risk factor for disseminated herpes zoster.[13] However, lymphopenia is a known risk factor of varicella-zoster virus reactivation, and it might be a contributory factor in our case.[14] Both mRNA and adenovirus vector vaccines generate virus-specific T cell responses in blood 2-4 weeks post vaccination.[15] However, vaccination against coronavirus disease 2019

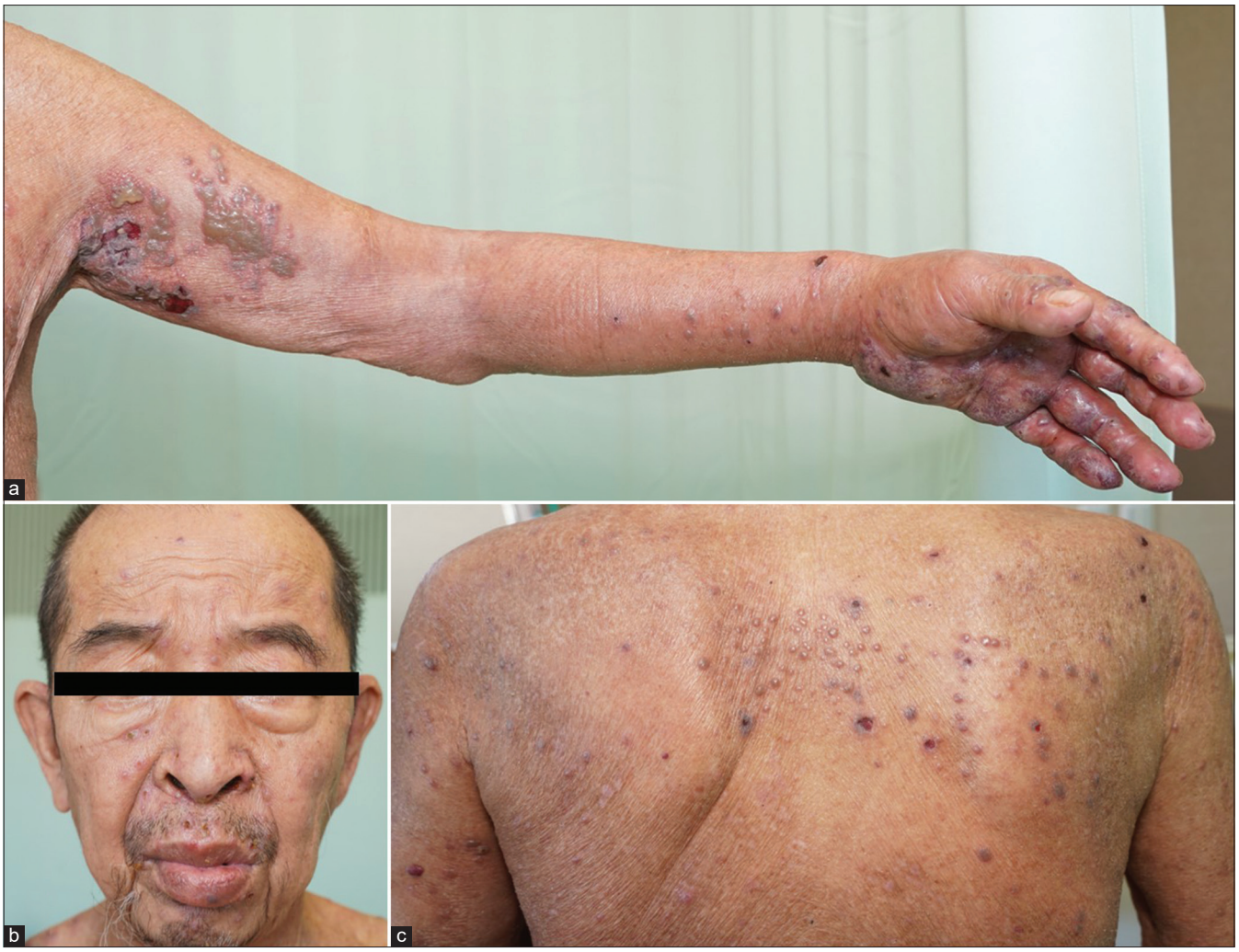

Figure 1: (a) Case 1: A 79-year-old male presented with unilateral vesicular eruptions on his left arm at the dermatome of C7, C8, and T1. (b) Case 1: The vesicles disseminated to face afterward. (c) Case 1: The vesicles spread to back after three days

may result in some kind of immunomodulation leading to varicella-zoster virus reactivation. Psichogiou *et al*. suggested that CD8+ cells may not be capable of controlling varicella-zoster virus temporarily due to the massive shift of naïve CD8+ cells towards anti-COVID-19 specific effector CD8+ cells, after Pfizer-BNT162b2 vaccination.[1] Furthermore, all our patients developed herpes zoster on the ipsilateral side of vaccination, consistent with literatures.[16,17] Though none of our cases received the second dose of their vaccine during our follow-up, van Dam *et al*. reported two cases who developed herpes zoster following first dose of severe acute respiratory syndrome coronavirus 2 BNT162b2 mRNA vaccine and remained uneventful after second dose.[18]

We have reported three cases of post-coronavirus disease 2019 vaccination-related herpes zoster We are unable to find any previous report documenting disseminated herpes zoster following Oxford-AstraZeneca vaccination. However, this association could be coincidental. Our report is limited by small sample-size.

This report highlights the need for increased vigilance regarding varicella-zoster virus reactivation after vaccination, especially in the susceptible elderly population as they are prone to suffer from postherpetic neuralgia for a longer period.

Declaration of patient consent

Institutional Review Board (IRB) permission obtained for the study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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