Herpes Zoster following SARS-CoV-2 vaccination – a series of four cases

Dear Editor,

The SARS-CoV-2 pandemic is a global public health crisis, with significant morbidity, mortality and socio-economical impacts. Vaccines were developed and granted emergency approvals by most drug agencies to tackle this crisis, but the safety profile of these vaccines is not fully clarified.

We present a series of four cases of varicella zoster virus (VZV) reactivation after vaccination against SARS-CoV-2, who presented at the Dermatology Department, Centro Hospitalar Universitário Lisboa Norte, Lisbon (Portugal), from 30 January 2021 to 30 April 2021. The characteristics of each patient are summarized in Table 1.

Two patients were administered Pfizer’s Comirnaty™ (New York, NY, USA) vaccine and two were given AstraZeneca Vaxzevria™ (Cambridge, UK) vaccine. The onset of complaints varied between 3 and 6 days following the first dose. Three patients presented with facial herpes zoster, and one patient had reactivation of VZV on an upper limb dermatome; on the same side, the vaccine had been administered (Fig. 1). The diagnosis was confirmed through polymerase chain reaction of a sample collected from the vesicles, which identified VZV in every case.

All patients improved under valacyclovir 1000 mg tid, and no immediate or long-term complications were observed. Patients 2 and 4 received the second dose of the vaccine without any occurrences.

Varicella zoster virus reactivation has been described in patients with COVID-191,2 and after vaccination against hepatitis A, rabies and influenza, suggesting a vaccine-induced immunomodulation.3 Recently, a series of VZV reactivation cases following Comirnaty™ administration in patients with rheumatological conditions under immunosuppressive and immunomodulatory treatments has been published, suggesting a possible link.4 While that report signals a possible link between one particular vaccine and VZV reactivation, the fact that all patients suffered from rheumatological conditions under immunosuppressant/immunomodulatory treatments limits generalization of these findings, particularly when the development programme of these vaccines did not identify this adverse reaction. In our series, all but one patient were otherwise healthy and not known to have any predisposing factor for VZV reactivation.

From a pathophysiological point of view, VZV reactivation in COVID-19 may be straightforward to explain, as a febrile condition where lymphopenia is common seems to be the ideal setting for VZV reactivation. On the contrary, the mechanisms behind VZV reactivation following SARS-CoV-2 vaccination are more elusive. A component of the vaccine might be responsible for this link; however, Comirnaty™ and Vaxzevria™ share few ingredients and rely on different technologies to lead to SARS-CoV-2 Spike-protein production by the cell. The only shared characteristic

Table 1 Characteristics of the reported cases of varicella zoster virus (VZV) reactivation following vaccination against SARS-CoV-2

| Patient # | 1 | 2 | 3 | 4 |
|-----------|---|---|---|---|
| Age       | 70 | 73 | 63 | 69 |
| Sex       | Female | Female | Female | Male |
| Medical conditions | Hallux valgus | Mechanical mitral valve prosthesis | – | Systemic lupus erythematosus Antiphospholipid antibody syndrome Plaque-type psoriasis Psoriatic arthritis Haemophilia A (mild) High Blood Pressure |
| Usual medication | – | Warfarin | – | Mycophenolate mofetil 500 mg bid Hydroxychloroquine 400 mg od Prednisolone 7.5 mg od Candesartan 32 mg od |
| Vaccine administered | Vaxzevria (AstraZeneca) | Vaxzevria (AstraZeneca) | Comirnaty (Pfizer) | Comirnaty (Pfizer) |
| Onset of VZV reactivation (days after first dose) | 3 | 4 | 6 | 3 |
| VZV reactivation site | Left V2 territory | Right V3 territory | Left C8 territory | Left V2/V3 territory |
| Prior History of Herpes Zoster | No | No | No | No |
| Other symptoms and adverse reactions | Local pain at administration site | Local pain at administration site | Local pain at administration site Fever for 24 h | Local pain at administration site |
between the two is indeed the expression of viral Spike protein to induce immune response.

Spike protein may have pleotropic effects in the host. This protein was shown to favour syncytium-mediated lymphocyte elimination\(^5\) and phenotypic transition of B-lymphocytes to macrophage-like cells with poor phagocytosis capability,\(^6\) These effects could be responsible for misbalancing the immune response that keeps VZV dormant. We stress that all cases occurred in individuals over 60 years old. Age is the major risk factor for VZV reactivation in 90% of the cases,\(^7\) and the absence of reports of Herpes Zoster in healthy younger individuals following SARS-CoV-2 vaccines may signify that these vaccines could be a contributing risk factor, but not a sufficient cause, for VZV reactivation.
New onset of mainly guttate psoriasis after COVID-19 vaccination: a case report

Editor

Psoriasis is a chronic, immune-mediated inflammatory disease with heterogeneous clinical manifestations. Various trigger factors like infections and drugs are known to elicit or aggravate psoriasis. Previously, a possible association of vaccination and the new onset (particularly guttate lesions) or exacerbation of psoriasis has been reported.1,2 Herein, we describe a case of mainly guttate psoriasis after a COVID-19 vaccination.

A 79-year-old female patient was referred to our department due to a disseminated itching psoriasiform rash, which had started 10 days after receiving the first injection with the COVID-19 vaccination Comirnaty® (BioNTech, Freiburg-strasse, Bern, Switzerland). There was no prior or family history of psoriasis or any other putative triggers (new intake of medication, underlying infections). Her past medical history revealed type-2 diabetes and hypertension and her daily medications (without any recent adaptations) included sitagliptin/metformin, empagliflozin, glitazide, bisoprolol, enalapril, aspirin and esomeprazole. On examination, there were numerous, disseminated, erythematous papules and partly scaly plaques mainly on the extensor surface of her arms, thighs (Fig. 1a,b), back and scalp. After some improvement with topical clobetasol propionate ointment once daily, the second dose of Comirnaty® was given, which again led to a flare-up particularly on her arms and legs. The patient is currently on treatment with topical calcipotriol/ betamethasone ointment and UVB phototherapy.

In order to characterize the skin lesions, histological [Haematoxylin & Eosin (H&E) staining] and immunohistochemical examinations of a lesional punch biopsy specimen were performed. Histopathological examination showed an acanthotic hyperparakeratosis alternating with orthokeratosis, as well as superficial perivascular lymphohistiocytic infiltrates with a few scattered neutrophils, consistent with guttate psoriasis (Fig. 1c). Immunohistochemical analysis using the avidin-biotin complex-alkaline phosphatase (ABC-AP) method was performed with following primary antibodies: CD1a (clone MTB1; Leica Biosystems, Nussloch, Germany), CD4 (clone 4B12; DakoCytomation, Glostrup, Denmark), CD8 (clone 4B1; Leica Biosystems), CD11c (clone 5D11; Novocastra, Muttenz, Switzerland), CD32 (clone EPR6657; Abcam, Cambridge, MA, USA), CD68 (clone PG-M1, DakoCytomation), CD163 (clone EDHU-1; Serotec MCA, Oxford, UK), CD303/BDCA2 (clone 124B.13, Dendritics,...