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LETTER TO THE EDITOR

Varicella-Zoster virus reactivation following SARS-CoV-2 immunization in two patients with leukemia

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To the Editor

In response to the coronavirus disease 2019 (COVID-19) pandemic, several vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have been approved for use.[1–3] BNT162b2 manufactured by Pfizer Inc. is the vaccine currently available for children and young adults in our hospitals and clinics. Monitoring for potential adverse vaccine events is particularly needed in high-risk patients excluded from initial vaccine clinical trials.[1] Varicella-zoster virus (VZV) establishes latency in sensory ganglia following primary infection with wild-type VZV or vaccine strain.[4,5] It is unclear if non-VZV immunization also can be associated with VZV reactivation.[6] We report two cases of VZV reactivation following SARS-CoV-2 immunization in patients with an underlying hematologic malignancy in Houston, Texas.

Case 1: A 17-year-old female with acute lymphoblastic leukemia (ALL) presented with a 1-month history of a vesicular rash. Two days after receipt of her first SARS-CoV-2 vaccine, she reported pain and redness over the right side of her back and subsequently developed a cluster of fluid-filled lesions. Five days after her second vaccine, she developed new lesions on her face, neck, and chest, and she was admitted to the hospital. She had primary VZV infection around 6 years of age. She was receiving methotrexate and 6-mercaptopurine, and had no recent changes to her immunosuppression or other identified stressors. During admission, her lowest absolute neutrophil count (ANC) was 520 cells/mm^3 and lowest absolute lymphocyte count (ALC) was 200 cells/mm^3. Vesicles on her forehead and neck were unroofed and the tissue was positive for VZV by polymerase chain reaction (PCR) and negative for herpes simplex virus (HSV). A biopsy of the skin lesions on her back was performed given the unusual black eschar (Figure 1). Viral, fungal, and bacterial cultures were negative. She was treated with intravenous acyclovir and then transitioned to oral valacyclovir to complete a 2-week course of therapy and subsequently received prophylactic dosing of valacyclovir.

Case 2: A 20-year-old male with relapsed ALL presented with right-sided facial weakness and oral lesions 17 days after his second SARS-CoV-2 vaccine. He reported a 1-day history of difficulty closing his right eye and drooling from the right-side of his mouth. His current medications included methotrexate, with a dose increase 3 days prior to presentation, and 6-mercaptopurine. He had a past history of VZV vaccination. On physical examination, he had oral lesions and a right-sided facial droop (Figure 1). Ophthalmologic examination revealed no ocular involvement. Magnetic resonance imaging of the brain demonstrated enhancement along the right seventh and eighth cranial nerves. Laboratory evaluation included lowest ANC of 1460 cells/mm^3 and ALC of 540 cells/mm^3. PCR testing of an oral lesion was positive for VZV and negative for HSV. He completed a 2-week course of valacyclovir with a steroid taper. In follow up 7 weeks later, he had residual right-sided facial weakness but no oral lesions.

We present two patients with underlying ALL who developed VZV reactivation following SARS-CoV-2 vaccination, indicating the need for increased vigilance in recognizing VZV reactivation in at-risk patients. Our patients demonstrated different clinical manifestations of their first episode VZV reactivation. One patient presented with disseminated Herpes zoster (HZ), while the other patient had Ramsay Hunt syndrome.

Abbreviation: ALC, absolute lymphocyte count; ALL, acute lymphoblastic leukemia; ANC, absolute neutrophil count; COVID-19, coronavirus disease 2019; HSV, herpes simplex virus; HZ, herpes zoster; PCR, polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; VZV, varicella-zoster virus.

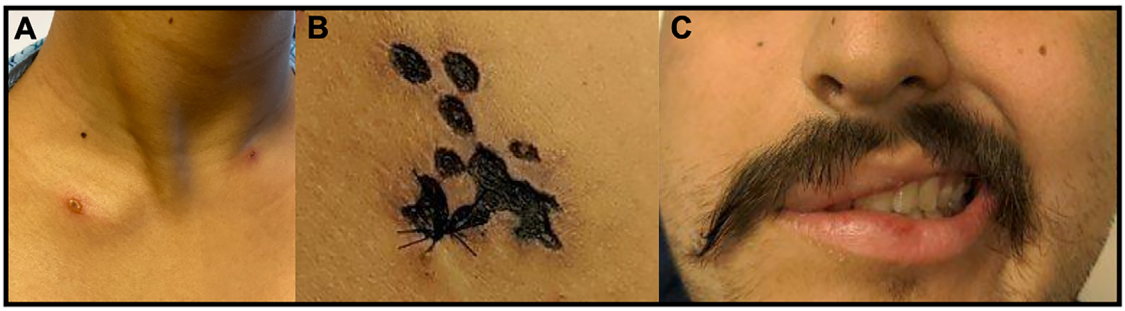

FIGURE 1 (A) Vesicular lesions present on the right clavicle and left lower neck. (B) Crusted black eschar along the right mid-back (suture present post biopsy). (C) Right facial droop when attempting to smile

There are multiple reports of VZV reactivation and the development of HZ in adults with COVID-19 infection.[7–10] A reduction in lymphocytes, especially CD3+ CD8+ lymphocytes, which can occur during infection with SARS-CoV-2, has been proposed as a potential mechanism triggering reactivation of herpesviruses.[7] Furer and colleagues published a case series of six adult patients with underlying rheumatologic conditions who developed HZ within a short timeframe following BNT162b2 vaccination.[10] Their report suggests the need for ongoing epidemiologic studies on the safety of mRNA-based COVID-19 vaccines, especially in immunocompromised patients, to clarify if there is a link with VZV reactivation.[10]

Our first patient described the appearance of skin lesions 2 days following her first SARS-CoV-2 immunization and 5 days following her second immunization, while the second patient had a more delayed presentation at 17 days after the second immunization. The reason for the difference in time to presentation is unclear. The onset of Ramsay Hunt syndrome may be more insidious than disseminated HZ; the appearance of vesicles in children with Ramsay Hunt is often delayed in comparison to adults.[11,12]

Additionally, both patients were immunocompromised which increases the likelihood of VZV reactivation. The incidence of HZ is five to six times higher in immunosuppressed children compared to nonimmunosuppressed children.[13] Patient two had an increase in methotrexate dosing 3 days prior to development of symptoms, which may have increased his risk. The observed timing of reactivation after vaccination in these patients could also represent a coincidence.

Our report is subject to several limitations. We would not have captured patients presenting outside of the Texas Children's Hospital system, nor patients who did not have a VZV PCR performed. We did not perform a comparison study between SARS-CoV-2 vaccinated and unvaccinated individuals to determine the incidence of VZV reactivation. While further studies are needed to determine if a causal relationship exists between COVID-19 vaccination and VZV reactivation, we recommend a heightened suspicion for HZ in recently vaccinated immunosuppressed patients presenting with vesicular lesions.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ETHICS STATEMENT

Informed consent was obtained and properly documented regarding use of the photographs in Figure 1.

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