Herpes Zoster and Varicella Encephalitis Following the Recombinant Zoster Vaccine

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PRACTICE **POINTS**

- Patients with chronic lymphocytic leukemia (CLL) are at risk for herpes zoster reactivation even with vaccination due to a decreased immune response. These patients may have an aberrant response due to immune cell dysregulation.
- It is important to increase monitoring of CLL patients for signs of viral reactivation and shift the focus to providing antiviral therapy quickly if herpes zoster symptoms occur.

To the Editor:

Reported adverse effects following the recombinant zoster vaccine (RZV) include pyrexia, myalgia, and fatigue.[1] We report the case of a patient who developed herpes zoster and subsequent varicella encephalitis within 8 days of receiving the second dose of the RZV.

A 75-year-old man presented to the emergency department with burning pain and pruritus involving the left hip and calf 2 days after receiving the second dose of the RZV. He had a history of chronic lymphocytic leukemia (CLL) and was being clinically monitored. He received the first dose of the RZV without complication 3 months prior. In the emergency department, he was diagnosed with "nerve pain," given acetaminophen, and discharged home; however, he continued to have worsening pain 8 days later followed by a vesicular eruption that wrapped around the left leg and was concentrated on the inner thigh/groin area in a dermatomal distribution. His primary care physician diagnosed him with herpes zoster and prescribed valacyclovir 1000 mg every 8 hours for 7 days. Two days later, the patient developed weakness and confusion and returned to the emergency department. Upon admission, computed tomography and magnetic resonance imaging/magnetic resonance angiography of the brain was normal. A lumbar puncture confirmed varicella encephalitis via a polymerase chain reaction assay. He was treated with intravenous acyclovir and discharged to a rehabilitation facility. His course was further complicated by a subarachnoid hemorrhage and normal pressure hydrocephalus. He did not require a shunt but continues to have memory impairment, weakness, and cognitive impairment. He is steadily improving with rehabilitative services.

The RZV is an inactivated vaccine composed of the varicella-zoster virus (VZV) glycoprotein E antigen and an adjuvant, $AS01_B$, that boosts both innate and adaptive immunity.[2] It was approved by the US Food and Drug Administration in 2017 for prevention of herpes zoster in adults aged 50 years or older. It requires 2 separate injections administered 2 to 6 months apart. Its efficacy for the prevention of cutaneous herpes zoster and postherpetic neuralgia is 97% and 80% to 91%, respectively. It was developed to improve on the existing zoster vaccine live, which contains a live attenuated virus, with efficacy ranging from 38% to 70%.[3]

The Centers for Disease Control and Prevention initially recommended the RZV for immunocompetent

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individuals or those taking low-dose immunosuppressant medications as well those who have recovered from an immunocompromising illness. In immunocompetent patients, reported adverse effects include injection site pain and redness, headache, myalgia, fatigue, shivering, fever, and gastrointestinal tract symptoms; however, when the vaccine first came out, many of the studies excluded patients with CLL.[4] Our patient's herpes zoster and varicella encephalitis occurred following administration of the second dose of the RZV. Herpes zoster occurs from declining VZV-specific cell-mediated immunity. Given that the vaccine contains inactive virus, it is unlikely that our patient's infection was the direct result of dissemination of the virus contained within the vaccine. The RZV specifically generates T-cell responses to the glycoprotein E subunit of VZV, which is thought to be responsible for the high levels of VZV-specific memory T cells with the RZV compared to the zoster vaccine live.[5] However, this response does not occur until after the second dose of RZV. Although our patient already had 1 dose of RZV, it was unlikely that he had a substantial number of glycoprotein E and VZV-specific memory T cells to combat virus reactivation. Additionally, his CLL, though mild, may have resulted in an aberrant T-cell response in the presence of already low VZV-specific lymphocytes, allowing for reactivation and dissemination of the virus. Since then, there has been more of an emphasis on looking at the immunogenicity elicited by the vaccine in patients with CLL—both those who are treatment naive and those treated with Bruton tyrosine kinase inhibitors. Both groups of patients have demonstrated reduced immunogenicity in response to RZV, leaving the opportunity for viral reactivation in this patient population.[6,7]

The safety of the RZV has now been demonstrated in patients with CLL.[7] However, even after RZV vaccination, patients with CLL are still at risk for herpes zoster reactivation and may have an aberrant response due to immune cell dysregulation. Our case demonstrates the need to increase monitoring of CLL patients for signs of viral reactivation and shift our focus to providing antiviral therapy quickly after symptom occurrence.

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