A Case of Herpes Zoster and Meningitis in a Twice-Vaccinated Healthy Adolescent

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Abstract

Since the adoption of the varicella-zoster virus (VZV) vaccine, the incidence of varicella infections of all types has declined. Although uncommon, local cutaneous herpes zoster secondary to vaccine-strain VZV has been well documented in healthy children. However, there are few reports of vaccine-strain VZV central nervous system disease in this same population. We present a case of a previously healthy twice-VZV vaccinated 14-year-old girl who presented with rash and headache who was found to have herpes zoster complicated by meningitis. Cerebrospinal fluid polymerase chain reaction confirmed zoster infection secondary to reactivation of vaccine-strain VZV. Her disease course and response to therapy are reviewed.

Keywords
- varicella-zoster virus vaccine
- varicella-zoster virus
- herpes zoster
- meningitis

Case Presentation

A previously healthy 14-year-old girl was transferred to our emergency department on day 4 of her illness with worsening headache and rash. Her symptoms had started with a frontal headache noted to be worse in the mornings. On day 3 of illness, she noticed a pruritic rash on her trunk and presented to an outside emergency department. The rash was noted to be vesicular and in a left truncal dermatomal distribution, not crossing midline. She was prescribed an unknown dose of valacyclovir for presumed herpes zoster and discharged home. However, she was unable to tolerate any oral doses of valacyclovir at home due to nausea and she presented again the following day to the same emergency department for evaluation. A review of systems was positive for nausea, weakness, and myalgias, but negative for neck stiffness, fever, chills, vision change, numbness, as well as any respiratory, gastrointestinal, or genitourinary symptoms. A brain magnetic resonance imaging was performed and showed no abnormalities. Lumbar puncture (LP) was attempted but was unsuccessful due to patient discomfort. She was given intravenous (IV) fluids, ketorolac 15 mg IV, metoclopramide 10 mg IV, and morphine 2 mg IV, and subsequently transferred to the Massachusetts General Hospital for Children (MGHfC) for further evaluation. Initial examination at MGHfC revealed a tired, but nontoxic-appearing adolescent with vital signs appropriate for her age. Notably, she was afebrile. She had multiple intact vesicles on an erythematous base with areas of confluence in a T5 dermatomal distribution, from just below her left breast wrapping around to her back. There were no signs of bacterial superinfection with no purulent drainage. Her neurologic exam was overall unremarkable including a
fundoscopic exam revealing a sharp disc on the left (right was unable to be visualized), intact cranial nerves 2 to 12, no nystagmus, normal tone and strength, and intact finger-to-
tongue testing. She denied exposure to, or infection with, primary varicella. Records from her primary care physician indicated that she received doses of varicella-zoster virus (VZV) vaccine at the age of 18 months and 12 years. In addition, she had confirmed immunity with a positive VZV immunoglobulin G (IgG) titer. Initial laboratory studies revealed peripheral white blood cell (WBC) count of 6.53 K/µL (72.8% neutrophils, 13.5% lymphocytes, 12.9% mono-
cytes, and hemoglobin of 9.6 g/dL with MCV 77.9. Inflamma-	ory markers were normal with erythrocyte sedimentation rate 17 mm/h and C-reactive protein 0.3 mg/L. Pediatric

Discussion

Since adoption of national recommendations for live-atten-
uated VZV vaccination in 1995, the incidence of primary varicella has dramatically declined. The effectiveness of a single-dose vaccine to prevent disease was found to be 85%, and is estimated to improve to 98% with the two-dose regimen recommended as of 2006.1 Concurrently, the inci-
dence of herpes zoster has declined in a similar fashion.2,3 However, the risk of VZV reactivation still remains, and should be considered in the appropriate clinical context. Ten-year postvaccine CDC surveillance data (1995–2005) identified cases of herpes zoster due to both wild-type and vaccine-strain VZVs,4 and there is a growing body of litera-
ture documenting VZV infection in previously immunized

Herpes zoster results from reactivation of dormant VZV after primary infection or vaccination. It typically activates in a single sensory dorsal root ganglion and causes a painful vesicular rash in a dermatomal pattern. Disseminated disease is less common but can include multiple organ systems. CNS manifestations of VZV can range in severity from mild reversible disease to death.

Advances in diagnostic techniques now allow us to easily identify VZV in CSF by PCR DNA amplification. With these improved techniques, there is increasing evidence to suggest that VZV-associated CNS disease is more common than previously thought. Several studies have now established VZV reactivation as a leading cause of viral meningitis and encephalitis.5–8

In a statewide study of CNS disease in California, the clinical presentations of VZV CNS infection included menin-
gitis (50%), encephalitis (42%), and acute disseminated

In addition, our patient was previously vaccinated, and VZV genotyping at the CDC identified vaccine-strain virus from her CSF. There are only a small number of reported cases of CNS infection due to vaccine-strain VZV in immunocom-
potent children.4–7 To our knowledge, ours is the first re-
ported case in a child who received two doses of the VZV

vaccine. Per current CDC guidelines, the first varicella vaccine should be administered between 12 and 15 months and the
second between 4 and 6 years; a minimum of 3 months should elapse between doses, but there is no maximum elapsed time. Our patient did not receive these doses per the recommended U.S. schedule, as she received her doses at the age of 18 months and 12 years.

Her presentation also reflects the likely different CNS manifestations in wild-type and vaccine-strain VZV cases. Similar to cases previously reported, our patient’s infection presented with meningitis alone. In contrast, wild-type VZV is most commonly associated with encephalitis. A possible underlying immunologic explanation has not yet been identified.

There are limited data to determine the optimal therapy for VZV CNS infection. The current recommendation by the Infectious Disease Society of America is 10 to 14 days of IV acyclovir for VZV encephalitis, but there are no clear recommendations for VZV meningitis.9 Our patient was treated for 7 days with IV acyclovir given her lack of viremia, immunocompetent status, and quick symptomatic improvement. In addition, she was discharged with an additional 14 days of oral valacyclovir, for a total of 21 days of antiviral therapy; this agent has been shown to have adequate CSF penetration and clinical efficacy against VZV encephalitis.10

In our case, there may have been an inappropriately decreased suspicion for disseminated VZV infection on initial presentation, as headache and rash were the only initial complaints. There was no fever, and she was a fully vaccinated, immunocompetent adolescent. Thus, there was a delay in diagnosis and treatment. Given high rates of routine immunization for VZV, there is likely to be an increase in the incidence of disease secondary to vaccine-strain VZV reactivation among both immunocompetent and immunocompromised children. Our case highlights the importance of considering VZV-related CNS disease in all children with suspicious history and physical exam, regardless of prior vaccination status.

References
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