A Rare Case of an Immunocompetent Male With Zoster Meningitis

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Abstract
Varicella zoster meningitis is an uncommon complication of herpes zoster, especially in immunocompetent patients. We report a case of a healthy 45-year-old male who developed aseptic meningitis as a result of reactivated varicella zoster virus infection. This case highlights the importance of remaining cognizant of varicella zoster virus as a cause of meningitis in not only the elderly or immunocompromised patients but also in patients who are healthy.

Keywords
viral meningitis, aseptic meningitis, CNS infections, zoster meningitis

Introduction
Varicella zoster virus (VZV) is a rare cause of viral meningitis in immunocompetent patients. In this case, we present an immunocompetent middle-aged man who presented with signs and symptoms of meningitis associated with dermatomal skin rash.

Case Presentation
A 45-year-old male with a past medical history of hyperlipidemia presented with complaint of headache and fever. Forty-eight hours prior to admission, he became febrile with a temperature of 101°F, lethargic, and developed headache and noticed rash on the left side of his back. Subsequently, the patient had myalgia, neck stiffness, nausea, and vomiting. He was taken to urgent care clinic where he was found to be confused and not able to answer questions appropriately. He was sent to the emergency room immediately thereafter. On arrival, the patient was alert, awake, and oriented to self, place, and time but drowsy. On physical examination, the patient had vesicular rash on the T10 dermatome (Figure 1) as well as mild neck rigidity. The patient was afebrile in the emergency room and had normal white blood cells count of 7.4. Influenza A/B antigens were negative. Computed tomography scan of brain without contrast and magnetic resonance imaging with contrast showed no acute findings. He was started on empiric antibacterial coverage with vancomycin and ceftriaxone as well as acyclovir after lumbar puncture was performed. Cerebrospinal fluid (CSF) analysis showed lymphocytic pleocytosis with 741 white blood cells, 97% lymphocytes, 3% neutrophils, glucose 41, and protein 296. CSF-polymerase chain reaction (PCR) was negative for herpes simplex virus 1 and 2 but VZV DNA was detected by the PCR in CSF. HIV-1/2 AG/AB was nonreactive and HIV-1/2 RNA was not detected as well. Antibiotics were stopped and acyclovir was continued. The patient improved clinically and was discharged home on a 14-day course of intravenous acyclovir with close follow-up at the outpatient infectious disease clinic (Figure 1).

Discussion
VZV, a member of the Herpesviridae family, is a highly contagious neurotropic virus that infects nearly all humans.1 Primary infection causes the characteristic skin rash with itchy blisters and pustules, while secondary reactivation infection causes a painful dermatomal rash that can be complicated by central or peripheral nervous system involvement and typically affects elderly and immunocompromised populations.

Following VZV reactivation and replication, the involved sensory ganglion exhibits intense inflammation and hemorrhagic necrosis.2 Zoster is a necrotizing inflammation of the spinal ganglion of the involved nerve that is

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in direct contact with CSF and rarely causes herpes zoster meningitis or encephalitis.

Per the Centers of Disease Control and Prevention, the lifetime risk of developing zoster is 33%, increasing to 50% in patients of 80 years of age due to cancers, especially leukemia and lymphoma, HIV infection, bone marrow or solid organ transplantation, and immunosuppressive medications.³ The overall annual incidence of zoster is about 0.46% and up to 1% in patients above the age of 80.⁴ Besides the aforementioned risk factors, the followings are associated with increased risk of herpes zoster development: being White, female, or physical trauma exposure.⁵,⁶ The most common complication of VZV is post-herpetic neuralgia, followed by zoster ophthalmicus or oticus. The development of central neurological complications of VZV reactivation including aseptic meningitis, encephalitis, or myelitis is relatively uncommon, especially in immunocompetent patients. A large tertiary hospital-based series studied the epidemiological characteristics of central nervous system (CNS) infection by VZV in patients older than 65 years of age and reported mean annual incidence of VZV CNS infection of 0.003%.⁷ On literature review, only a handful of cases have been reported of VZV reactivation in immunocompetent patients, most of which involved adult or elderly patients.⁸⁻¹²

For proper diagnosis, CSF analysis using molecular biology tests such as PCR—to detect viral particles is considered a cornerstone.¹³ However, a negative result does not rule out the infection, especially if the CSF sample was obtained after the initiation of antiviral therapy, hence the importance of CSF analysis prior to treatment. Although a vesicular rash with dermatomal distribution is a typical symptom of VZV, some cases of VZV meningitis without skin lesions have been described.¹⁴ VZV aseptic meningitis CSF findings typically includes the following: lymphomonocytic pleocytosis of <500 cells/μL, moderately elevated total proteins, and normal lactate levels.¹⁵ It is important to ascertain that reactive pleocytosis and some degree of meningeal irritation frequently associates with otherwise uncomplicated herpes zoster, which can occur in 40% of cases.¹⁶ Other diagnostic clues include an increased production of anti-VZV antibodies in the CSF suggesting active disease (serum/CSF VZV antibody ratio ≤20) or (CSF antibody/serum antibody)/(CSF albumin/serum albumin) ≥2.

Guideline recommended therapy for VZV meningitis is intravenous acyclovir 10 to 15 mg/kg every 8 hours for 10 to 14 days. Oral valacyclovir 2 g every 6 hours for at least 10 to 14 days can be considered in patients with no other risk factors.¹⁷ Valacyclovir is metabolized into acyclovir in the intestine and liver and has the same antiviral activity as acyclovir.¹⁸ When choosing between valacyclovir and acyclovir, we have to keep in account the 50% inhibitory concentration, drug concentration in the CSF, and their potential adverse effects. As intravenous acyclovir is associated with more side effects compared with oral valacyclovir, including CNS toxicity, rarely permanent CNS, and renal damage as well as it is associated with an increased cost of health care, it is considered as a treatment option.¹⁹ That being said, more research needs to be done as there are not many reported cases of patients successfully treated with oral valacyclovir. One percent to 6% of individuals will experience the second episode of zoster. However the recurrence of zoster meningitis is unknown.²⁰ The overall prognosis of VZV meningitis is good, especially in healthy individuals and rarely causes any sequelae.²¹

**Follow-up and Outcome**

The patient successfully completed 2 weeks of treatment without any side effects at the outpatient infectious disease clinic. The patient symptoms completely resolved.

**Conclusion**

VZV meningitis is an infrequent cause of aseptic meningitis. However, with increasing cases of VZV infection, it is crucially important to suspect VZV infection as a potential cause in an immunocompetent patient with or without the typical vesicular dermatomal rash. Early antiviral therapy initiation is warranted to prevent further neurologic sequelae and ensures good prognosis.

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**Author Contributions**

Mohammed Ali Faluk, Shradhadevi Makadia, and Ramy Abdelmaseih wrote the original draft of the paper. Mohammed Ali Faluk participated in gathering the data for the case and also compiling the draft. All authors read and approved the final manuscript.
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Ethics Approval
Our institution does not require ethical approval for reporting individual cases or case series.

Informed Consent
Verbal informed consent was obtained from the patient for their anonymized information to be published in this article.

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