

# Varicella Zoster Meningitis with Hypoglycorrhachia on Cerebrospinal Fluid (CSF) Analysis in a Young Immunocompetent Host without a Rash

Authors' Contribution:  
Study Design A  
Data Collection B  
Statistical Analysis C  
Data Interpretation D  
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**Conflict of interest:** None declared

**Patient:** Female, 44  
**Final Diagnosis:** Varicella zoster meningitis  
**Symptoms:** Headache  
**Medication:** —  
**Clinical Procedure:** —  
**Specialty:** Infectious Diseases





**Objective:** Unusual clinical course  
**Background:** Varicella zoster virus (VZV) is a common viral infection, with primary infection presenting as fevers and pruritic vesicular rash. After staying dormant in the dorsal root ganglia, reactivation can lead to secondary infection. Meningitis is a rare a complication of VZV infection.

**Case Report:** We report a case of a 44-year-old woman with no past medical history, presenting with severe frontal headache without meningeal signs or fevers, found to have VZV meningitis. CSF analysis revealed hypoglycorrhachia and she was treated successfully with combination of intravenous acyclovir and oral valacyclovir.

**Conclusions:** VZV meningitis can present with subtle clinical signs and symptoms and should be considered as a possible etiology for headaches without identifiable cause.

**MeSH Keywords:** Headache Disorders • Herpesvirus 3, Human • Meningitis, Aseptic

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## Background

Varicella zoster virus (VZV), a member of the herpes virus family, is a common cause of viral infections [1]. Primary infection transmitted via skin inoculation or respiratory droplets presents as crops of pruritic vesicular rash with centripetal spread and a high-grade fever [2]. Secondary infection occurs as a result of reactivation of VZV that was dormant in the dorsal root ganglia. Common complications of infection include post-herpetic neuralgia, ocular involvement, motor neuropathy, superimposed bacterial skin infections, and meningitis [1]. VZV meningitis is commonly seen in immunocompromised hosts, with symptoms of fever and rash. Here, we report an uncommon presentation of VZV meningitis in a 44-year-old immunocompetent woman who presented with isolated headache without rash or fever.

## Case Report

A 44-year-old woman without any significant past medical history, presented with a chief complaint of severe headache for 1 day. She was evaluated at an urgent care clinic and a computed tomography (CT) scan of the head was performed, which was negative for any intracranial process, and she was discharged with a prescription for acetaminophen/butalbital/caffeine and Meloxicam. As her headaches did not improve, she presented to our medical center after 3 days.

Upon arrival, she described her headaches as constant, dull, frontal, non-radiating, 10/10 in severity, and a “driving knife-like pain in the head” when standing. It was not related with any specific activity and she was unable to perform her daily activities. She did report mild nausea, photophobia, and phonophobia, but denied any confusion, tearing of the eyes, eye redness, changes in vision, fevers, chills, neck stiffness, rash, or body aches. She did not report associated auras, fortification spectrum, vertigo, or seizures. She did not report any sick contacts, recent travel, weakness, or tingling or numbness of the extremities. She had not been taking any medications or oral contraceptives. She was married and had 2 teenage children. She did not endorse any history substance abuse, smoking cigarettes, or drinking alcohol.

Vitals signs were within normal limits on presentation, including blood pressure of 97/55 mmHg and temperature of 37°C. On neurological examination, there was no scalp tenderness, jaw claudication, nuchal rigidity, or photophobia. Jolt test and Kernig’s and Brudzinski’s signs were negative. Cranial nerves were intact. She did not exhibit any focal weakness, range of movement was within normal limits, and her sensation to soft touch and cerebellar signs were normal. Triceps, patellar, and Achilles deep tendon reflexes were 1+ and equal bilaterally.

A comprehensive skin examination, including that of genitalia, did not reveal any rashes, lesions, or erythema. A repeat CT scan of the head and CTA (computed tomography angiography) of head did not show any signs of intracranial pathology. MRI of the brain with and without contrast did not show any tumors, sinus thrombosis, or evidence of periventricular plaques suggestive of multiple sclerosis. Complete metabolic panel and complete blood count were normal. A urine pregnancy test was negative. HIV testing was negative. A lumbar puncture was undertaken for further evaluation of the headache. Spinal fluid showed normal red blood cell (RBC) count, and elevated white blood cell (WBC) count of 422 cells/ $\mu$ L (normal <5 cells) with lymphocytic predominance, glucose of 35 mg/dL (ref range: 45–80 mg/dL), and protein of 225 mg/dL (ref range: 14–45 mg/dl). Serum glucose drawn before lumbar puncture was 110 mg/dL, resulting in a CSF-to-serum glucose ratio of 0.3. Gram staining of spinal fluid did not show any organisms and cultures remained negative. Meningitis panel by polymerase chain reaction (PCR) was positive for varicella zoster virus. Additional CSF studies were unremarkable. She was started on intravenous (IV) acyclovir, upon which symptoms started to improve. She was discharged after receiving 5 days of IV acyclovir and was instructed to complete outpatient oral valacyclovir 1000 mg 3 times per day for 14 days. On follow-up in our continuity clinic, her headache had completely resolved without any neurological sequelae.

## Discussion

Varicella zoster virus (VZV), a member of the herpes virus family, is a common cause of viral infections in the USA, with an annual incidence of approximately 1.5–3 cases per 1000 persons, and nearly 90% of all adults have serological evidence of prior infection [1,3]. Varicella zoster virus (VZV) infection is categorized into primary and secondary forms of the disease. Primary VZV (chickenpox) is most often characterized by crops of pruritic vesicular rash with centripetal spread and acute neuritis [2] along with high fever. Primary infection is transmitted via direct skin inoculation or respiratory droplets [1,3]. The virus infects local T cells, replicates first in regional lymph nodes, and eventually spreads into the epidermis [4–6].

VZV migrate via sensory nerves to establish latency in dorsal ganglia of sensory nerves [5]. Secondary VZV reactivates in sensory ganglia and typically involves the thoracic and lumbar dermatomes. Reactivation of virus presents with abnormal skin sensation of tingling, itching, and pain, with eventual cutaneous eruption of maculopapular rash in unilateral dermatomal pattern [3]. This rash progresses to clusters of clear vesicles that eventually ulcerate and crust [3]. In the present case, the patient did not have any skin rash and denied any prior symptoms suggestive of herpes infection. Common complications of

infection include post-herpetic neuralgia, ocular involvement, motor neuropathy, superimposed bacterial skin infections, and meningitis [2,7]. In a review of 859 patients with herpes zoster infection, 100 patients had complications within 60 days of infection, with risk of complications having a positive correlation with age [7].

Aseptic meningitis is defined as clinical meningitis with negative bacterial cultures, with the most common cause being enterovirus infection [8]. Varicella zoster is a less common but notable cause of aseptic meningitis, seen in 8% to 13% of cases [8,9]. Meningitis is a rare complication of VZV infection, seen in approximately 0.5% of patients diagnosed with recent zoster infection [10]. The pathophysiology of VZV spread to the central nervous system is still debated. It has been suggested that the virus can spread via afferent nerve fibers, to nerves roots close to the central nervous system, allowing for transport into the meninges [11]. Other theories propose hematologic spread leading to infection of neurons and blood vessels of the central nervous system [11].

The predominant symptom of varicella zoster meningitis is headache [12]. Other symptoms may include fever, neck stiffness, or rash, but these were absent in our case. In various literature reviews, the typical VZV rash is absent in 33% to 60% of patients, creating a diagnostic challenge [10–12]. PCR of the CSF shows hypoglycorrhachia, with elevated CSF WBC and protein. A retrospective study of 620 patients with meningitis showed that 19% had hypoglycorrhachia on CSF PCR; of these patients, the etiology was viral in 15%. Responsible viruses included West Nile virus (WNV), herpes simplex virus (HSV), varicella zoster virus (VZV), cytomegalovirus (CMV), and acute HIV infection [13]. In contrast to our patient, who was immunocompetent and did not report symptoms other than headache, patients with hypoglycorrhachia were more likely to be immunosuppressed, present with vesicular/pepetchial rash, and have a positive history of intravenous drug use [13]. The pathophysiology of hypoglycorrhachia is unclear, and current theories suggest that it is multifactorial. Possible mechanisms include changes in the blood brain barrier, altering glucose entry into the subarachnoid space, increased rate of transportation of glucose across arachnoid villi, increased glycolysis by leukocytes and bacteria, and hypermetabolism of glucose by the CNS [13].

Spernovasilis et al. reported a similar case of a young male with frontal headaches and chills, and was found to have VZV meningitis with hypoglycorrhachia on CSF analysis. Compared

to our case, that patient exhibited additional clinical signs of meningitis, with neck stiffness and low-grade fevers. However, diagnosis was made with PCR on CSF, and treatment with acyclovir was initiated [14]. Habib et al. and Pasedag et al. both reported cases of VZV meningitis with severe headaches with additional signs such as nausea and vomiting. These were also diagnosed and treated in a similar manner [15,16]. These cases highlight the subtle symptomatology that can be seen in VZV meningitis, creating a diagnostic challenge for clinicians.

Molecular methods for diagnosis of viral encephalitis were first described in the late 1990s. DeBiasi et al. published an article in 2004 discussing this novel technique [17]. Routine CSF studies were rarely able to identify specific viral etiological agents prior to the development of CSF PCR. A large multicenter retrospective study showed that CSF PCR was positive for VZV in 100% of cases, while CSF culture was only positive in 33% [18].

There are various recommendations for the treatment of VZV meningitis. Recently, it was suggested to use 2 g of valacyclovir 3 times per day for treatment [19]. Treatment with oral valacyclovir 1 g 3 times per day has also been shown to maintain a therapeutic concentration of acyclovir in the CSF [20,21]. Our patient was effectively treated with a lower dose of valacyclovir, with no clinical complications, and had resolution of symptoms on follow-up.

## Conclusions

In conclusion, our immunocompetent young female patient had a nonspecific presentation of aseptic meningitis with a debilitating headache without meningeal signs or dermatologic manifestations. Our case highlights the subtle presentation of VZV meningitis and the diagnostic challenge it can present. VZV meningitis should be considered as a differential diagnosis of patients with headaches, even if they present without the suggestive rash, fevers, or neurological signs. Hypoglycorrhachia can also be seen in nonbacterial meningitis, and PCR should be done on CSF analysis to ensure nonbacterial causes in appropriate clinical settings. Further studies should be done to establish the pathophysiology of hypoglycorrhachia in viral meningitis, as well as the appropriate dosage for treatment with valacyclovir.

## Conflict of interests

None.

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