



Case report

Varicella-zoster virus meningitis with hypoglycorrachia in a young immunocompetent adult without rash: A case report and literature review



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ABSTRACT

Overt aseptic meningitis rarely complicates varicella-zoster virus (VZV) reactivation in young and immunocompetent adults. Many of the cases of VZV meningitis are associated with an exanthem. We describe an otherwise healthy 36-year-old adult who had aseptic meningitis without skin rash, caused by reactivation of varicella-zoster virus. Cerebrospinal fluid (CSF) analysis revealed lymphocytosis, increased total protein, and low glucose. Diagnosis was made by polymerase chain reaction in CSF. The present case highlights the fact that VZV should be considered as a cause of aseptic meningitis with hypoglycorrachia in healthy and young individuals, even in the absence of an exanthem.

Introduction

Varicella-zoster virus (VZV) is a human neurotropic virus, member of the *Herpesviridae* family. It has the ability to remain dormant in cranial and dorsal root ganglia [1]. Two clinical syndromes are caused by this virus. The primary infection (chickenpox) usually occurs during childhood and is extremely contagious, characterized by fever, malaise, and a vesicular rash [2]. Reactivation of VZV results in herpes zoster (shingles), with dermatomal distribution of pain and rash, and it is usually a disease of older or immunocompromised people [1,2]. Central nervous system (CNS) involvement may occur during primary infection or reactivation, and may include meningitis, encephalitis, meningoencephalitis, vasculopathy, myelitis, Guillain-Barré syndrome, and retinal inflammatory disorders [1,2].

Here, we present the case of a previously healthy young man with aseptic meningitis without rash as a result of reactivated VZV infection, in whom cerebrospinal fluid (CSF) analysis revealed hypoglycorrachia.

Case presentation

A 36-year-old Caucasian male presented to our hospital with a 4-day history of persistent frontal headache and low-grade fever, with no other symptoms. He had an episode of varicella infection in his childhood, but no history of zoster since then. The rest of his medical history was unremarkable. Apart from paracetamol, no other medications had

been taken in the previous days. He was an active smoker with a 10-pack-year history, with no use of alcohol or illicit drugs. His family history was insignificant. He was married, lived in an urban area, worked as a refrigeration technician, and with no contacts with animals.

Initially, the patient was evaluated by an otorhinolaryngologist, without findings from the ear, nose and throat examination, but neck stiffness was noted, and the patient was referred to the emergency department. On examination, he was alert and oriented. His body temperature was 37.6 °C, while the rest of his vital signs were normal. Neck stiffness was present, but no other neurological abnormalities were detected. The remainder of the clinical examination, including skin, respiratory and cardiovascular system, was normal.

A chest x-ray and a computed tomography of the head and sinuses were carried out and showed no abnormalities. Laboratory tests revealed a white blood cell (WBC) count of 6.1 k/uL (neutrophils: 61.3%, lymphocytes: 24.5%, monocytes: 11.7%, eosinophils: 2.2%, basophils: 0.3%) and a platelet count of 149 k/uL. The serum biochemical parameters of kidney and liver function were normal. C-reactive protein and erythrocyte sedimentation rate levels were within normal range also. Blood and urine culture were drawn and serology for human immunodeficiency virus (HIV) was obtained. A lumbar puncture (LP) was performed in the emergency room and yielded clear cerebrospinal fluid (CSF), with 400/uL WBC (94% lymphocytes), 25/uL red blood cells (RBC), a total CSF protein of 177 mg/dL, and a CSF glucose of 45 mg/dL (serum glucose of 90 mg/dL), with a CSF to serum glucose ratio of 0.5.

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Gram stain, Ziehl–Neelsen stain and Indian ink stain were negative, while CSF cultures were sent. CSF volume was insufficient for performing polymerase chain reaction (PCR) studies. The patient was started on intravenous ceftriaxone and acyclovir and he was admitted to the internal medicine department with the diagnosis of probable aseptic meningitis.

On day 3 of hospitalization, the patient was afebrile, while the headache and the neck stiffness had resolved. Blood, urine and CSF cultures obtained on admission did not demonstrate any bacterial growth, and ceftriaxone was stopped. The HIV serology was negative too. A second LP was performed in order to collect a CSF sample for neurotropic virus PCR and assess the need for continuing acyclovir treatment. Repeated LP revealed WBC count of 667/uL (93% lymphocytes), RBC count of 30/uL, total protein level of 94 mg/dL, and a glucose level of 38 mg/dL (serum glucose of 94 mg/dL), with a CSF to serum glucose ratio of 0.4. The PCR analysis of the CSF herpes simplex virus (HSV) I and II was negative, but VZV DNA was detected. The patient received a total of 8 days of intravenous acyclovir and he was discharged with instructions for an additional 6-day course of oral valacyclovir and for performing a magnetic resonance imaging (MRI) of the brain as an outpatient. On his follow-up visit two weeks later, the patient was in a good health condition, while the MRI showed no abnormalities.

Discussion

VZV meningitis is an uncommon complication of herpes zoster [3]. Nevertheless, VZV represents one of the commonest etiological agent for aseptic meningitis [4–6]. The progress of the technology has allowed a more detailed attribution of central nervous system (CNS) disorders to VZV. PCR and other molecular amplification methods are characterized by high sensitivity and specificity in detecting viral DNA in CSF, and have become essential tools in the diagnostic armory [1]. In contrast with VZV encephalitis or meningoencephalitis, VZV meningitis is associated with a favorable clinical outcome in immunocompetent hosts, and the need for treatment with antiviral agents in these patients is controversial [6].

It is well established that aging causes a multitude of changes in the immune system leading to numerous defects, and to a subsequent vulnerability to pathogens [7]. Additionally, disease-related or iatrogenic immunosuppression has deleterious effects on host defense [8]. Defects in specific functional compartments of the immune system are associated with susceptibility to specific infectious agents [8]. Herpes zoster is most frequent in the elderly and in immunocompromised patients [1,2]. The reason relies on the fact that VZV-specific, cell-mediated immunity declines with age or immunosuppression, and it is the adaptive T cell response that is crucial for preventing the reactivation of the latent virus [7–9]. A recent study demonstrated that the incidence of herpes zoster was twice as high in immunocompromised than in immunocompetent hosts, and that higher incidences were observed among individuals with severe immunosuppression [10]. Higher incidences were also observed among women and older patients [10].

Herpes zoster is manifested by a unilateral dermatomal rash, which is painful and/or pruritic. It starts as papules and quickly evolves into vesicles or bullae. Occasionally, a dermatomal distribution of pain and/or pruritus occurs in the absence of an antecedent skin eruption. This condition is known as zoster sine herpette [1]. The dormant virus has also the ability, during its reactivation, to travel from the ganglia to the central nervous system, without concurrent skin manifestations [11]. Indeed, in cases of VZV meningitis, rash can be absent in a significant proportion of patients [5,12–14].

The CSF analysis in viral meningitis typically includes lymphocytic pleocytosis, a slightly elevated protein level, and a normal glucose level. A CSF hypoglycorrhachia is defined as CSF glucose equal or less than 45 mg/dL, and is usually detected in bacterial, tuberculous, and fungal meningitis [15]. Less common causes of hypoglycorrhachia

include acute syphilitic meningitis, *Mycoplasma pneumoniae* meningitis, primary amebic meningitis, meningial cysticercosis, carcinomatous meningitis, subarachnoid hemorrhage, sarcoidosis, rheumatoid meningitis, and lupus myelopathy [16]. Viruses that may cause low CSF glucose levels when they invade meninges are mumps and, occasionally only, HSV, enteroviruses, lymphocytic choriomeningitis virus and VZV [13,14,16]. It must be emphasized that CSF glucose level may be falsely low in case of concurrent hypoglycemia. A serum glucose must be drawn before the LP, and a CSF to serum glucose ratio must be calculated. A normal ratio is around 0.6, and ratios less than 0.5 are considered abnormal [15].

We report an unusual presentation of VZV meningitis with hypoglycorrhachia in previously healthy young adult without a rash. Only few similar adult cases have been previously reported [17–19]. Mayo and Booss [17] reported four young patients without exanthem and with clinical and serological diagnosis of VZV meningitis. Three of them had low CSF glucose, while the other patient had an abnormal CSF to serum glucose ratio. All had a favorable outcome. Habib et al. [18] presented an immunocompetent 26-year-old woman without a rash who was diagnosed with VZV meningitis using PCR in CSF, with low CSF glucose and CSF to serum glucose ratio. The patient was successfully treated with intravenous acyclovir. Pasedag et al. [19] reported an 18-year-old previously healthy man without exanthem and with molecular and serological diagnosis of VZV meningitis, presented with hypoglycorrhachia and treated successfully with acyclovir and valacyclovir.

Conclusion

Our case emphasizes the importance of considering reactivated VZV as a cause of aseptic meningitis in young and immunocompetent individuals, even in the absence of an exanthem. It is also highlight the fact that VZV meningitis can be accompanied by hypoglycorrhachia. The widespread use of molecular methods in CSF analysis allows the prompt recognition of CNS involvement during the course of this viral disease and the early initiation of treatment.

Declarations of interest

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Consent

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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