

CASE REPORT

Varicella-zoster virus aseptic meningitis: an atypical presentation in an immunocompetent male patient

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Abstract

Varicella-zoster virus (VZV) reactivation causes a relatively common disease in immunocompromised patients characterized by rash and radiating pain. Aseptic meningitis is a rare complication of VZV infection and commonly is associated with exanthem and neurological signs. We present an atypical case of VZV meningitis in a healthy 56-year-old male who was initially presented with persistent headache as the only symptom. Anti-VZV immunoglobulin G titer both in serum and in cerebrospinal fluid (CSF) and the polymerase chain reaction (PCR) CSF analysis revealed VZV infection. Our case highlights the importance of considering VZV aseptic meningitis in immunocompetent individuals even in the absence of the typical presentation of meningitis. Screening techniques such as CSF, PCR as well as anti-VZV antibodies in CSF show that VZV meningitis is a common cause of aseptic meningitis and allows the early recognition of CNS involvement in the VZV infection.

INTRODUCTION

Viral meningitis is the most common cause of aseptic meningitis. The most commonly recognized pathogens are Enterovirus, Herpes simplex virus-1 (HSV1), Herpes simplex virus-2 (HSV2), varicella-zoster virus (VZV) and Human immunodeficiency virus (HIV; [1]). VZV is the third most frequent causal agent of viral meningitis [2]. The clinical manifestations of the central nervous system (CNS) infection from VZV include aseptic meningitis, encephalitis, cerebral infarct with concomitant granulomatous vasculitis, myelitis and multiple cranial neuropathies [1, 2]. These neurological disorders represent the resurgence of latent VZV in trigeminal ganglia and in the ganglia of the posterior roots resulting in dispersal of the infection in the CNS [3]. The most common complication is meningitis. In these patients, viral antigens or DNA are often detected in the CSF [4]. It is

known, that CNS complications from VZV are more common in immunocompromised patients [5]. Rarely, immunocompetent people may also be affected, commonly with primary clinical features of rash and neurological symptoms.

Here in, we report the case of a 52-year-old healthy Caucasian male, who was assessed in the Emergency Department (ER) due to headache since the last 4 days. Physical history and examination revealed no rash and no signs of meningeal irritation such as neck stiffness. The polymerase chain reaction (PCR) CSF analysis revealed VZV infection.

CASE REPORT

A 52-year-old Caucasian male with an unremarkable past medical history, working as foreman, visited the ER, complaining

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Table 1: Cerebrospinal fluid analysis results

Parameter	Results	Normal
WBC (mm ³)	374	0–5
	75% Lymphocytes,	5 Lymphocytes
	10% Polymorphs	0 Polymorphs
glucose (mg/dl)	57	45–80 (2/3 of Serum)
Protein (mg/dl)	87.6	15–50
GRAM staining	Negative	Negative
CSF culture	Negative	Negative

for frontal retrobulbar headache, progressively deteriorating for 4 days, not remitting with paracetamol. At the same time he reported weakness, malaise, myalgias and low back pain, but no fever. On physical examination, the patient was alert and fully orientated, without signs of discomfort and with normal vital signs. No neck stiffness was present while other signs of meningeal irritation were absent. There was not any rash on his body.

No abnormalities on laboratory tests were noticed, the inflammatory markers were: white blood cells 7640 (72% neutrophils) and C-reactive protein 1.17 mg/dl. Fundoscopy and brain CT were normal and lumbar puncture was done due to persistent headache. Analysis of the cerebrospinal fluid is showed in Table 1.

The patient was admitted to the Department of Internal Medicine and he underwent immediately IV treatment with ceftriaxone 2 g bid and acyclovir 10 mg/kg every 8 h.

Serology investigation for HSV1, HSV2, Epstein–Barr virus (EBV), Cytomegalovirus (CMV) and HIV was negative. Regular screening for HSV1/2 and VZV, with an algorithm applied by the Microbiology Laboratory in all CSF with elevated cells and/or protein, revealed the presence of VZV DNA. Retrospectively the same CSF was examined for the presence of specific immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies for VZV. Only IgG antibodies were detected 577 mIU/ml (normal values <165/mIU/ml), a titer that increased to 1263 mIU/ml in a subsequent sample taken after 8 days. Anti-VZV IgG titer was also very high in serum (13.530 mIU/ml, normal values <165 mIU/ml). PCR in CSF for West-Nile virus, CMV and EBV was also negative. A brain magnetic resonance imaging was performed without showing any intracranial abnormalities, such as bleeding, infarction, abscess or malignancy. The patient had no signs of sinusitis or temporal arteritis. Blood, urine and CSF cultures were negative for common pathogens.

Treatment was modified according to above test results and only IV acyclovir was continued for a total of 14 days. The patient remained afebrile during entire hospitalization with remission of the headache on Day 4. After completion of treatment, repeated lumbar puncture was performed with negative CSF PCR for VZV and the patient was discharged from the hospital.

DISCUSSION

The affection of VZV in the CNS can produce a wide variety of neurologic disease. Both immunocompetent and immunocompromised patients may suffer from VZV neurological complications, but these appear to be more frequent and severe in the latter group. The clinical manifestations of VZV encephalitis

include two types, meningoencephalitis and vascular disease. Meningoencephalitis is characterized by normal brain MRI (2) In contrast, the vascular disease type is characterized by non-specific ischemia, hemorrhagic lesions and multiple lesions in the white matter. Reports of VZV meningitis have increased in recent years, in the context of the increased use of PCR for detection of VZV in CSF. VZV reactivation accounts for approximately 5–29% of cases of acute aseptic meningitis [2].

Here, we present an atypical manifestation of VZV meningitis in an immunocompetent patient without suggestive rash, fevers or neurological signs; except a mild persistent headache as the sole symptom. In various literature reviews, there are many cases in immunocompetent individuals that also support the existence of a VZV meningitis without a rash, called VZV Sine Herpete [6–8]. In addition, Nam described a case of VZV meningitis with only headache [9].

Since the findings in CSF are not specific for the diagnosis of VZV infection it is advisable to identify CSF PCR VZV (considered test of choice for diagnosis). Anti-VZV antibodies in the CNS (of which a significant titer increase, during the course of disease indicates the production of intrathecal antibodies) can confirm the diagnosis as well [10]. The finding of the persistent headache in our case, the CSF analysis and the exclusion of other related pathologies led us to the diagnosis of VZV meningitis.

Traditionally VZV meningitis has been treated with IV acyclovir in accordance with the Infectious Disease Society of America treatment guidelines [7]. Recently, the use of oral valacyclovir was suggested as it has also been shown to maintain a therapeutic concentration of acyclovir in the CSF [3]. Prevention of VZV infections through vaccination is a priority to avoid the significant burden of its incidence and complications.

CONCLUSION

Our case highlights the importance of considering VZV aseptic meningitis in immunocompetent individuals when assessing headache of unidentifiable cause even in the absence of the typical symptoms of meningitis. Clinicians should be aware of this clinical entity and consider it in the differential diagnosis with a high suspicion index. The widespread use of molecular methods in CSF analysis allows the early recognition of CNS involvement in the VZV infection and clinicians must not harbor any reservations in ordering it.

CONFLICT OF INTEREST STATEMENT

None declared.

FUNDING

None.

ETHICAL APPROVAL

Not required, since this is not an experiment involving humans or animal. Informed written consent to publish this case report has been obtained from the patient. A copy of the written consent is available for review by the Editor-in-Chief of the journal on request.

CONSENT

Informed consent was taken from the patient prior to publication.

GUARANTOR

Dimitrios Vellisaris is the guarantor of this manuscript.

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