Case report

Varicella-Zoster meningitis with normal CSF cellularity: A rare case report

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ABSTRACT

Varicella-zoster virus (VZV) meningitis is one of the manifestations of VZV reactivation which usually presents with fever, headache, and is sometimes preceded by a dermatomal vesicular rash. CSF analysis is the cornerstone investigation in helping to identify the causative organism or in orienting the physician toward a possible agent. CSF analysis in Viral meningitis usually reveals lymphocytic pleocytosis. However, normal CSF analysis with viral meningitis—despite being rare—has been reported especially with bacterial causes. Therefore, a first CSF puncture cannot rule out infection and a second one might be warranted if there is still high suspicion of viral meningitis with no diagnosis made by PCR. Here we present a case of an 89-year-old female who had signs and symptoms of meningitis with normal CSF analysis. However, polymerase chain reaction (PCR) was positive for VZV. The patient was treated accordingly, and she recovered fully.

Introduction

Varicella-zoster virus (VZV) presents with many neurological complications after reactivation, the most common being a dermatomal vesicular eruption that is usually preceded by prodromal pain, itching, or tingling. Meningitis in immunocompetent patients is considered a known complication of VZV. It often manifests with a headache, fever, and sometimes a rash that may present 3–5 days after meningitis. This is along with lymphocytic pleocytosis in CSF analysis [1]. However, some cases in the literature have recently described viral meningitis with no pleocytosis such as Enterovirus and Herpes Simplex Virus [2,3]. We hereby present a case of VZV meningitis in an elderly patient along with the dermatomal rash and normal CSF findings.

Case presentation

An 89-year-old female patient with a history of hypertension and asthma presented with a severe left-sided occipital headache that has started three days prior to hospitalization. The headache was persistent, very severe in intensity, did not respond to analgesics. The patient denied any vomiting, fever, photophobia, or decrease in vision. Regarding the patient’s past medical history, it should be noted that her asthma was well controlled by a salbutamol inhaler as needed, hence no ED visits nor hospitalizations for asthma were reported. She was not on systemic steroids and didn’t receive pulse steroid therapy before. Upon further review of her vaccination history, she has not received the varicella vaccine before.

On physical examination: the patient was alert and oriented, had left jaw angle tenderness, left occipital and temporal scalp tenderness, with no rash overlying the temporop-occipital area. She had periorbital swelling after exposure to diclofenac sodium, which she took over the counter as topical treatment one day before admission, even though the patient has documented a history of allergy to diclofenac potassium. There were two noticeable 1 cm erythematous papules over the left eyelid only. However, on the second day of admission, the patient developed a papulovesicular rash on the left side of the forehead and upper eyelids. Moreover, Kernig and Brudzinski signs were negative but there was limited mobility of the neck with tenderness.

Vital signs on presentation: Temp Oral: 36.7 °C, Heart Rate: 91 beat/min, Resp Rate: 17 breath/min, systolic blood pressure: 154 mmHg, diastolic blood pressure: 77 mmHg, oxygen saturation: 99% on room air. Laboratory results on presentation summarized in Table 1. The patient was assessed by an ophthalmologist for left
eyelid swelling and rash, and he mentioned a vesicular rash over the eyelid that does not involve lid margins or conjunctiva. The cornea was clear with no staining, with dense nuclear cataract, and no signs of zoster ophthalmicus were appreciated.

Head CT without contrast (Fig. 1) showed Age-related parenchymal atrophic changes, otherwise, the study was unremarkable. Head MRI, MRV, MRA were also done, and they showed age-related changes along the cerebral sulci and ventricles, extensive periventricular and deep white matter ischemic gliotic changes, and few chronic lacunar infarctions were seen. Intracranial arteries and Dural sinuses were unremarkable with no radiologic evidence of arterial stenosis, aneurysm, or venous thrombosis. Ultrasound Doppler of both temporal arteries showed normal caliber arteries with normal wall thickness. The right artery wall measures 2.0 mm and the left measures 1.8 mm. Normal PSV and flow patterns were noted on both sides, overall, the findings were not compatible with temporal arteritis.

CSF analysis results showed Positive VZV PCR with normal cellularity, the results are summarized in (Table 2). VZV serology done retrospectively two days after the lumbar puncture revealed positive IgG antibodies in the serum with a simultaneous absence of IgM, no titters were available as the assay used in our department micro IgG antibodies in the serum with a simultaneous absence of IgM, no

Table 1
Summarizes blood lab test at the day of admission.

| Lab Test                  | Value       | Normal range         |
|---------------------------|-------------|----------------------|
| White Blood count (WBC)   | 12.8        | (4–10) * 10³/µL      |
| Hemoglobin (Hgb)          | 11.8        | (12–15) g/dl         |
| Platelets (PLTs)          | 380         | (150–400)* 10³/µL    |
| Absolute Neutrophils count| 3.8         | (2–7) * 10³/µL       |
| Absolute lymphocytes count| 7.5         | (1–3) * 10³/µL       |
| Urea                      | 3.5         | (2.5–7.8) mmol/L     |
| Creatinine                | 62          | (44–80) µmol/L       |
| Sodium                    | 136         | (133–146) mmol/L     |
| Potassium                 | 3.9         | (3.5–5.3) mmol/L     |

![Fig. 1. CT head: showed Age-related parenchymal involutional changes including dilated ventricular system.](image)

vesicular rash she developed, whilst waiting for CSF results. After confirming the diagnosis by PCR, the treatment was continued for 14 days. During her stay, her headache was controlled with oral tramadol. The initial dose was 50 mg three times per day, but the requirements decrease to once daily by the end of her stay.

Follow up: The patient got better, her hospital course was unremarkable, she completed her acyclovir course and was discharged with no pain and improved rash.

Two weeks after discharge, a follow up by the general medicine clinic confirmed that the patient was getting better regarding her skin rash, however, she was suffering from bouts of burning like pain in the left periorbital area, therefore, she was started on oral gabapentin 300 mg three times a day for postherpetic neuralgia management. Two weeks later in a subsequent medicine clinic follow-up, the patient reported improvement of the burning pain, no rash was seen on examination, and her gabapentin dosage was reduced to 300 mg once a day.

**Discussion**

VZV is one of the alpha-herpes viruses that usually cause mild to moderate presentation with disseminated vesicular rash in the primary infection. After reactivation VZV can cause a wide range of neurologic diseases, with herpes zoster and post-herpetic neuralgia being the most frequent. Meningitis is a more severe manifestation of VZV reactivation [1,4]. VZV meningitis is more prominent in immunocompromised states and older age patients. Patients mostly present with headaches, fever, lethargy, and sometimes rash that usually presents several days after the local pain [1]. Our patient presented with a severe left occipital headache and developed a rash six days after the onset of the headache.

After suspecting meningitis, initial CSF data (WBC, glucose, and protein) may help guide clinicians before a microbiological workup is done. CSF findings of lymphocytic pleocytosis usually predict a viral infection. While increased CSF lactate and decreased glucose ratio are useful predictors of bacterial infections [5], WBC count in VZV meningitis is usually around 302 cells/mm³ [6]. Our patient's CSF results showed no pleocytosis with normal glucose and protein.

Several studies have recently discussed cases of central nervous system infection with normal CSF cellularity. A recent systematic review found that most of the cases mentioned in the literature across all age groups were bacterial [99 of 124]. Whereas viral and fungal infections caused infection with normal cytology at a lower rate [7]. The absence of pleocytosis has been described with several viruses, but not well described in VZV. Whole-brain irradiation was associated with normal CSF cytology results as discussed by Jakob

Table 2
Summarizes CSF analysis.

| Lab test                  | Value       | Normal range         |
|---------------------------|-------------|----------------------|
| WBC (white blood cell)    | 1           | (0–5)/µL             |
| RBC (Right blood cell)    | 0           | (0–2)/µL             |
| Glucose                   | 4.05 Blood  | (2.22–3.89) mmol/L   |
|                            | Glucose was |                      |
| Protein                   | 0.44        | (0.15–0.45)          |
| Oligoclonal bands         | Negative    |                      |
| IgG index                 | 0.5         | (0.3–0.6)            |
| Latex Angulation for      | Negative    |                      |
| Cryptococcus              |             |                      |
| Tuberculosis (TB) PCR     | Negative    |                      |
| Gram stain and Culture    | No Growth   |                      |
| Cytomegalovirus (CMV) PCR | Negative    |                      |
| Human Herpes Virus (HSV- 6)PCR |          |                      |
| Herpes Simplex Virus (HSV-1 and 2) PCR | Negative | |
| Enterovirus PCR           | Negative    |                      |
| Varicella-Zoster Virus PCR| Positive    |                      |
of further investigations [14]. That’s why it is important to conduct powerful studies that reassess the diagnostic yield of CSF analysis in order to help guide clinicians more towards decision making. While emphasizing at the same time on maintaining a suspicion of CNS infection regardless of normal CSF cytology, especially in highly symptomatic patients. A repeat CSF puncture can be difficult due to the invasive nature of the test. Nevertheless, we emphasize that a single lumbar puncture with normal CSF cytology cannot rule out meningitis. And if no diagnosis was made with culture or PCR, physicians should consider repeating the test, especially if an infection is suspected clinically or the patient continues to deteriorate [7,15].

Ethical approval

Approved.

Consent

Written consent is available upon request.

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CRedit authorship contribution statement

Bana Sabbagh: Manuscript writing, literature review, and approval of the final manuscript. Mohammad Najdat Seijari: History and physical, manuscript writing and editing, case identification and conceptualization, literature review. Mhd Kutaba Albuni: manuscript writing and editing and corresponding author. Munsef Barakat: History and physical, case follow up. Gamal B Alfitori: Case selection, case identification and Conceptualization, obtain informed written consent, prescribing medicine, clinical follow up.

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Declaration

We declare no conflict of interest.

Conflicts of interest

No Conflict of interest.

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