Journal of Community Hospital Internal Medicine Perspectives

Volume 14 | Issue 6 Article 17

2024

An Atypical Case of Herpes Simplex 1 Meningitis

Nadim Ojaimi
MedStar Health Internal Medicine Residency Program, nadim.ojaimi@gmail.com

Sofia Zhang
MedStar Health Internal Medicine Residency Program

Marcos Wolff
MedStar Health Franklin Square Medical Center, Department of Infectious Disease

Christopher James Haas
Georgetown University School of Medicine, Department of Internal Medicine

Recommended Citation

Ojaimi, Nadim; Zhang, Sofia; Wolff, Marcos; and Haas, Christopher James (2024) "An Atypical Case of Herpes Simplex 1 Meningitis," *Journal of Community Hospital Internal Medicine Perspectives*: Vol. 14: Iss. 6, Article 17.
DOI: 10.55729/2000-9666.1413
Available at: https://scholarlycommons.gbmc.org/jchimp/vol14/iss6/17

CASE REPORT

An Atypical Case of Herpes Simplex 1 Meningitis

Nadim Ojaimi [a,*], Sofia Zhang [a], Marcos Wolff [b], Christopher J. Haas [a,c]

[a] MedStar Health Internal Medicine Residency Program, USA
[b] MedStar Health, Department of Infectious Disease, USA
[c] Georgetown University School of Medicine, Department of Internal Medicine, USA

Abstract

Herpes simplex virus (HSV) is well known to cause Central Nervous System (CNS) infections, ranging from more common HSV-2 viral meningitis to the more rare and severe HSV-1 encephalitis. Here we present an atypical case of aseptic meningitis due to HSV-1. Intriguingly, despite the potential severity of HSV-1 infections, the patient had an uncomplicated course with only mild symptoms that resolved with conservative management alone. This case report aims to provide a frame of reference for the non-specific presentation of a patient with uncommon HSV-1 meningitis.

Keywords: Herpes simplex virus, HSV-1, Encephalitis

1. Introduction

Aseptic meningitis is defined as meningeal inflammation in the setting of negative cerebrospinal fluid (CSF) bacterial cultures; it is most commonly due to a viral infection.[1,2] Even though non-polio enteroviruses are the most common cause of viral meningitis in the United States, herpesviruses remain a significant culprit.[3] Typical meningeal symptoms are milder in comparison to bacterial meningitis and include headache, photophobia, and nuchal rigidity. Most cases of HSV meningitis are associated with HSV-2,[2] which are usually benign, self-limited, lack genital lesions, and without long-term sequalae. In contrast, HSV-1 is more commonly associated with encephalitis, an inflammation of the brain usually caused by infection or autoimmune etiology.[4] HSV-1 encephalitis is generally more severe with a mortality rate up to 70% if left untreated[1] and survivors often suffer from long-term neurological sequelae such as dysphasia, amnesia, and behavioral disturbances.[4] Presenting symptoms include fever, altered level of consciousness, seizures, and focal neurological deficits secondary to temporal lobe lesions[4] due to HSV-1's ability to induce apoptosis in the CNS.[4] However, viral anti-apoptotic genes, such as the ICP10PK gene, are found in HSV-2 and protect the CNS from apoptosis, which explains the lack of severe complications.[5]

HSV-1 encephalitis, unlike the case presented here, is often treated with antiviral therapy, however the benefits of antiviral treatment for HSV-1 meningitis in an immunocompetent patient remains poorly characterized in current literature.[6]

2. Case Description

A 37-year-old Caucasian female with history of insulin-dependent diabetes mellitus, hypothyroidism, and attention deficit hyperactivity was in her usual state of health until ten days prior to presentation at which time she experienced thick, malodorous vaginal discharge, dysuria, urinary frequency, intermittent chills, and nausea. She presented to her primary care physician 5 days after the development of her symptoms and was prescribed nitrofurantoin and a dose of fluconazole. Three days after taking the medication, while reporting improvement in her vaginal discharge and dysuria, she developed generalized weakness and a progressively worsening bifrontal headache that was associated with photosensitivity and worsening nausea. She reported no fevers, chills, neck stiffness and had no focal neurological deficits, or joint pain. She reported no recent travel or other exposures. Similarly, the patient reported no prior

Received 20 April 2024; revised 14 August 2024; accepted 29 August 2024.
Available online 2 November 2024

* Corresponding author.
E-mail address: Nadim.ojaimi@gmail.com (N. Ojaimi).

https://doi.org/10.55729/2000-9666.1413

herpetic diseases or genital ulcers. As a result of her new and ongoing symptoms, she presented to the emergency department (ED) for further management and evaluation.

In the ED, her vitals were unremarkable except for mild tachycardia (101 beats per minute) and a low-grade fever (38.0 °C). Physical examination was otherwise unremarkable. Laboratory diagnostics including CBC and BMP were unremarkable. Urinalysis demonstrated trace blood, leukocyte esterase, and mild pyuria (11–15 WBC/hpf), and rare bacteria. A non-contrast head CT was unremarkable. Given the fever, headache, and photophobia, a lumbar puncture was done and showed elevated opening pressure (36 cm H_2O) which lead to resolution of her headache. Studies were significant for a lymphocytic pleocytosis and elevated protein (Table 1). CSF cultures were negative. Cytology demonstrated atypical cells including abundant lymphocytes, with scattered plasma cells, neutrophils, and monocytes. Initial Biofire® was negative for Cryptococcus but positive for non-specific HSV-1/HSV-2 (Table 2), and confirmatory PCR was sent for further speciation. HIV was negative. A brain MRI with venography demonstrated no evidence of meningeal enhancement, infarct, venous sinus thrombosis, or masses.

Table 1. Cerebrospinal fluid studies.

Appearance	Slightly cloudy
Color	Colorless
Xanthochromia	Present (Abnormal)
WBC	1554/mm3 (0–5)
Segmented Neutrophils	2% (0–7)
Lymphocytes	95 % (28–96)
Monocytes	3 % (16–56)
RBC	27/mm^3 (0–1)
Proteins	119 mg/dL (15–45)
Glucose	43 mg/dL (40–70)
Culture	No growth at 24 h

Table 2. BioFire film array meningitis/encephalitis panel.

Escherichia coli K1	Negative
Haemophilus influenzae	Negative
Listeria monocytogenes	Negative
Neisseria meningitidis	Negative
Streptococcus agalactiae	Negative
Streptococcus pneumoniae	Negative
Cytomegalovirus (CMV)	Negative
Enterovirus (EV)	Negative
Herpes simplex virus 1 (HSV-1)/Herpes simplex virus 2 (HSV-2)	**Positive**
Human herpesvirus 6 (HHV-6	Negative
Human parechovirus (HPeV)	Negative
Varicella zoster virus (VZV)	Negative
Cryptococcus (C. neoformans/C. gattii)	Negative

The patient was administered two doses of acetazolamide for her elevated opening pressures. Given the rapid resolution of her symptoms and no concerns of being immunocompromised, she was not treated with antivirals. Patient was discharged with outpatient follow-up. The dedicated PCR study speciated HSV-1 a few days post-discharge. Patient was re-contacted and reported improvement in most of her symptoms and instructed to follow-up with infectious disease clinic, however, she was lost to follow-up.

3. Discussion

HSV is one of the most common causes of meningoencephalitis with a high morbidity and mortality.[7] Typically HSV-1 has a more aggressive course and is usually associated with encephalitis, while HSV-2 typically causes aseptic meningitis and has a more benign course.[3,8,9]

Most of the current data and management derives from HSV-2 meningitis, which usually presents with lymphocytic pleocytosis <1000 WBC/mm3, elevated protein (50–300 mg/dL), normal glucose (40–70 mg/dL) and a normal to mildly elevated opening pressure.[3,10] Our patient had marked pleocytosis (1554 WBC/mm3) and elevated opening pressure (36 cm H_2O), which is unusual for aseptic meningitis, and had a benign course nonetheless. Although the patient was eventually found to have the virulent HSV-1, she had no signs of encephalitis and improved significantly with supportive therapy alone.

Currently, only limited observational studies and a few case reports have been published regarding the management of HSV-1 meningitis.[11] There are no comprehensive guidelines for managing HSV-1 and 2 associated meningitis. Immunocompetent individuals without complications, such as urinary retention or weakness, are mainly managed through supportive care.[6,11] When treated with a short course of antiviral therapy, immunocompromised patients with HSV meningitis had fewer neurologic sequelae when compared to immunocompromised patients who did not receive antiviral treatment,[6] while immunocompetent patients with HSV meningitis typically improve with or without specific antiviral therapies.[12] However, if indicated, HSV-2 meningitis is managed with intravenous acyclovir at a dose of 10 mg/kg every 8 h for a duration of 10–14 days. Subsequently, transitioning to oral valacyclovir 1 g three times daily is feasible based on clinical improvement.[13] In contrast to meningitis, encephalitis's treatment duration typically lasts for 14–21 days, necessitating exclusive intravenous therapy.[14]

The management of recurrent lymphocytic meningitis (previously known as Mollaret's meningitis) caused by HSV-2 with oral therapy should be evaluated individually due to the scarcity of supporting evidence.[9,15-17]

4. Conclusion

HSV-1 commonly manifests as encephalitis; however, it can also present atypically, leading to aseptic meningitis. Therefore, HSV-1 should be considered in the differential diagnosis. This case underscores the rarity of HSV-1 causing meningitis, emphasizing the need for further research and heightened clinical awareness to enhance understanding and management of such cases.

Disclaimers

None.

Ethics approval

Not applicable.

Funding

Not applicable.

Conflict of interest

The Authors have no conflict of interest to declare.

References

1. Tyler KL. Herpes simplex virus infections of the central nervous system: encephalitis and meningitis, including mollaret's. *Herpes*. 2004;11(Suppl 2):57A–64A.
2. Hansen AE, Vestergaard HT, Dessau RB, et al. Long-term survival, morbidity, social functioning and risk of disability in patients with a herpes simplex virus type 1 or type 2 central nervous system infection, denmark, 2000-2016. *Clin Epidemiol*. 2020;12:745–755. https://doi.org/10.2147/CLEP.S256838.
3. Ihekwaba UK, Kudesia G, Mckendrick MW. Clinical features of viral meningitis in adults: significant differences in cerebrospinal fluid findings among herpes simplex virus, varicella zoster virus, and enterovirus infections. *Clin Infect Dis*. 2008;47(6):783. https://doi.org/10.1086/591129.
4. Ellul M, Solomon T. Acute encephalitis - diagnosis and management. *Clin Med*. 2018;18(2):155–159. https://doi.org/10.7861/clinmedicine.18-2-155.
5. Jameson JL, Kasper DL, Longo DL, et al, 1107, 1114t. *Harrison's principles of internal medicine*. 21st edn vol. 1. New York; Chicago; San Francisco: McGraw Hill; 2022:1474–1475, 1478t.
6. Noska A, Kyrillos R, Hansen G, Hirigoyen D, Williams DN. The role of antiviral therapy in immunocompromised patients with herpes simplex virus meningitis. *Clin Infect Dis*. 2014;60(2):237. https://doi.org/10.1093/cid/ciu772.
7. Whitley R, Baines J. Clinical management of herpes simplex virus infections: past, present, and future. *F1000Res*. 2018;7. https://doi.org/10.12688/f1000research.16157.1. eCollection 2018. doi: 10.12688/f1000research.16157.1.
8. Tansarli GS, Chapin KC. Diagnostic test accuracy of the BioFire® FilmArray® meningitis/encephalitis panel: a systematic review and meta-analysis. *Clin Microbiol Infection*. 2019;26(3):281. https://doi.org/10.1016/j.cmi.2019.11.016.
9. Dylewski JS, Bekhor S. Mollaret?s meningitis caused by herpes simplex virus type 2: case report and literature review. *Eur J Clin Microbiol Infect Dis*. 2004;23(7). https://doi.org/10.1007/s10096-004-1164-y.
10. Read SJ, Kurtz JB, Ltd M. Laboratory diagnosis of common viral infections of the central nervous system by using a single multiplex PCR screening assay. .
11. Eisenstein LE, Calio AJ, Cunha BA. Herpes simplex (HSV-1) aseptic meningitis. *Heart Lung*. 2004;33(3):196–197. https://doi.org/10.1016/j.hrtlng.2002.12.002.
12. Kaewpoowat Q, Salazar L, Aguilera E, Wootton SH, Hasbun R. Herpes simplex and varicella zoster CNS infections: clinical presentations, treatments and outcomes. *Infection*. 2015;44(3):337. https://doi.org/10.1007/s15010-015-0867-6.
13. Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. *MMWR Recomm Rep (Morb Mortal Wkly Rep)*. 2021;70(4):1–187. https://doi.org/10.15585/mmwr.rr7004a1.
14. Tunkel AR, Glaser CA, Bloch KC, et al. The management of encephalitis: clinical practice guidelines by the infectious diseases society of America. *Clin Infect Dis*. 2008;47(3):303–327. https://doi.org/10.1086/589747.
15. Carmena Carmena J, Macià Soler M, Cremades Mira A, Alcaraz Soriano MJ. Herpes simplex 1 virus mollaret meningitis. *Rev Clínica Española*. 2004;204(8):418–419. https://doi.org/10.1157/13064316. https://www.ncbi.nlm.nih.gov/pubmed/15274766.
16. Steel JG, Dix RD, Baringer JR. Isolation of herpes simplex virus type 1 in recurrent (mollaret's) meningitis. *Trans Am Neurol Assoc*. 1981;106:37–42. https://www.ncbi.nlm.nih.gov/pubmed/6294952.
17. Aurelius E, Franzen-Röhl E, Glimåker M, et al. Long-term valacyclovir suppressive treatment after herpes simplex virus type 2 meningitis: a double-blind, randomized controlled trial. *Clin Infect Dis*. 2012;54(9):1304–1313. https://doi.org/10.1093/cid/cis031.