Herpes simplex meningitis presenting as headache in pregnancy: A case report

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ABSTRACT

Background: There are few case reports of meningitis caused by herpes simplex virus (HSV) as the initial presentation in a pregnant patient, making pregnancy management and delivery planning challenging for obstetricians encountering this patient presentation.

Case: A 35-year-old parous woman at 35 weeks of gestation presented to the emergency department with worsening headache and signs consistent with meningitis. Due to her history of SLE, a rheumatology consultation was arranged, although her flare symptoms were not consistent with her initial presentation. Neurology was consulted after she developed fever and abnormal labs consistent with meningitis. She was started on broad-spectrum antibiotics while waiting for lumbar puncture results. The latter indicated the patient was positive for HSV-2 IgG, suggesting a recurrent process. She denied a personal history of HSV infection, although she had a positive unspecified HSV IgM titer upon chart review. The patient was transitioned to intravenous acyclovir and responded well. Upon clinical improvement, she was transitioned to oral antiviral therapy and subsequently discharged home. After consultation with the pediatrics and pediatric infectious disease departments, vaginal delivery was deemed to be safe. However, the patient elected for primary cesarean.

Conclusions: Providers encountering a patient with an unrelenting headache in the absence of other causes should have a high suspicion of meningitis, regardless of clinical HSV history.

1. Introduction

There are few case reports of herpes simplex virus (HSV) meningitis presenting in a pregnant patient, making pregnancy management and delivery planning challenging for obstetricians encountering this patient presentation. An understanding of proper management of HSV is crucial for obstetricians, as 15.9% of reproductive-aged women are seropositive [1]. HSV is a double-stranded DNA virus, whose primary target is epithelial cells and it disseminates by hematogenous spread. The virus has a complex genome, encoding over 80 polypeptides and several glycoproteins. The differentiation of glycoprotein g, specifically, permits the expression of either HSV-1 or HSV-2 [2]. This case report concerns a pregnant patient with a history of three preterm deliveries and without a history of genital herpes who initially presented at 35 weeks of gestation to the emergency department for a headache not responding to medication. After extensive multidisciplinary workup, she was diagnosed with herpes meningitis.

2. Case Presentation

A 35-year-old parous woman at 35 weeks of gestation presented to the emergency department with worsening headache not responding to medication, photosensitivity, back pain, unilateral calf pain, and fever at home. She had a personal history of migraines, sickle cell trait, and systemic lupus erythematosus (SLE). Her obstetric history was notable for three prior preterm deliveries, preeclampsia in a previous pregnancy, and pyelonephritis in this pregnancy for which she had been hospitalized earlier.

She was normotensive, afebrile, tachypneic, and tachycardic. Her initial neurological exam was unremarkable, and she was noted to have a supple neck without any nuchal rigidity. She had mild to moderate left costovertebral angle tenderness. Her initial workup was notable for a
slightly increased serum white blood count at 13.8 and negative urinalysis. A head computerized tomography scan without contrast was negative for hemorrhage, herniation, hydrocephalus, and intracranial pathology. A lower-extremity Doppler scan and chest x-ray were also negative.

The emergency medicine physician consulted rheumatology, neurology, infectious disease, and obstetrics/gynecology. Rheumatology did not think the episode was related to her history of SLE as her typical flare symptoms were arthralgias. In addition, since her diagnosis ten years prior, she had been asymptomatic and without flares from a SLE standpoint. When neurology initially examined the patient, they documented a negative Kernig and Brudzinski sign. However, on repeat examination, findings consistent with mild meningeal irritation was observed. They performed a lumbar puncture and the patient was started on empiric ampicillin, cefepime, and vancomycin, as recommended by the infectious disease team. The patient was transferred to labor and delivery’s triage. While in triage, the patient had a reactive fetal non-stress test and negative sterile speculum exam. A group B streptococcus (GBS) swab was collected as well. Given her history of preterm labor, a sterile vaginal exam was performed, and the patient was found to be 1 cm dilated. She was 3 cm dilated on hospital day 1.

The patient’s cerebrospinal fluid meningitis/encephalitis panel ultimately resulted HSV-2 IgG positive, suggesting a recurrent process. The patient denied a clinical history of genital or oral herpes. Infectious disease recommended discontinuation of the patient’s cefepime and vancomycin, but continued her ampicillin to cover a potential GBS infection. She was started on intravenous acyclovir 10 mg/kg every 8 h. On hospital day 2, the patient’s headache was noted to be improving. On day 3, her GBS resulted negative, and ampicillin was discontinued. By day 5, her headache had completely resolved and she was transitioned to valacyclovir. On day 6, she was discharged home in good condition. Given the initial concerns for preterm labor, a repeat sterile vaginal exam was repeated prior to discharge. The patient was found to be unchanged at 3 cm dilated.

The patient continued valacyclovir until delivery at 39 weeks of gestation. She was extensively counseled on the mechanism of delivery by the pediatrics and obstetrics teams. Both teams counseled the patient that there was a very low likelihood of vertical transmission at the time of vaginal delivery in the absence of vaginal lesions. She was counseled that her laboratory results suggested a recurrent process despite her lack of a clinical HSV infection prior to her diagnosis of meningitis. The patient was uncomfortable with any potential risk of transmission via vaginal delivery and strongly desired a primary cesarean to minimize risk. This was felt to be reasonable by both teams and a primary cesarean was scheduled for 39 weeks. Her procedure was uncomplicated from a surgical standpoint and a viable male infant weighing 3635 g was delivered with Apgar scores of 8 at one minute and 9 at five minutes.

Despite low suspicion from the pediatrics team of vertical transmission of her infection, a thorough exam and careful monitoring of the neonate was performed, both of which were unremarkable. The patient and her neonate had an unremarkable hospital course and were discharged home in good health.

3. Discussion

Classification of HSV infection is important for assessing and counseling on risk of vertical transmission and can be challenging in a patient without a history of lesions.

Once this patient’s meningitis and encephalitis panel resulted positive for HSV-2 infection, her providers attempted to classify her infection. Herpes infections can be classified into primary, non-primary first episode, or recurrent infections. Primary infections occur when a lesion is positive for a strain of the herpetic virus, without any evidence of serum antibodies. In non-primary first-episode infections, a lesion is positive for one strain of herpes, while the patient has serum antibodies to the other viral strain. Patients suffering from recurrent infections have antibodies to the same virus causing their current infection [1].

By classifying infections, providers can help stratify risk to the neonate. If a patient has a primary infection at the time of delivery, there is a 40–80% chance of vertical transmission to the neonate. If a patient were to have HSV secretions at the time of delivery, there is a 1.2% chance of neonatal infection if delivered via cesarean and a 7.7% chance of infection with vaginal delivery [1]. However, complicating matters is the fact that 60–80% of neonatal HSV infections occur following asymptomatic primary infections. Although the risk of transmission to the neonate is lower in cesarean sections, a study found that providers would have to perform 1580 cesarean sections to prevent one case of neonatal HSV infection [2].

On chart review, this patient was seen to have had a positive, unspecified IgM titer over a decade earlier. When she presented to her primary care manager for sexually transmitted infection testing, a physical exam was not performed nor was documentation of any symptoms related to a potential sexually transmitted infection made in her note. In addition, she reported never having symptoms of outbreaks. This lack of documentation and absence of a specific IgM antibody rules the classification of the patient’s infection. However, the presence of an HSV-2 IgG antibody suggests a recurrent process. In addition, HSV-1 serum antibody testing was performed on the patient during her admission, which resulted negative for HSV-1 IgG antibodies. Therefore, this patient’s infection was classified as a recurrent infection.

Given the rarity of HSV infection presenting as meningitis in pregnant patients, the route of delivery was thoroughly discussed with the patient. Since she had a negative sterile speculum exam and had the opportunity to begin antiviral suppressive therapy four weeks before delivery, it was reasonable to counsel her on vaginal delivery of her neonate as a safe delivery route. In addition, given the fact that her infection was classified as a recurrent infection, the risk of neonatal vertical transmission was significantly lower than if she had had a primary infection. However, cesarean section was also a reasonable delivery route given the paucity of literature related to neonatal outcomes in this circumstance. In addition, as neonatal morbidity and mortality can be grave for those infected with herpes, it was reasonable to offer cesarean section to an individual with an atypical presentation of herpes.

Another challenge in this case was determining fetal benefits of prolonging antiviral treatment. The patient was counseled that maternal treatment of her infection could be effective in treatment of her fetus if there were intrauterine involvement. However, intrauterine involvement is exceedingly rare, at 1 in 200,000 pregnancies [2]. In terms of neonatal outcomes, there is little literature regarding HSV central nervous system infections in pregnancy. However, one published case series demonstrated overall positive outcomes for infants without treatment or intervention [3].

Once the patient began to clinically improve, providers sought to identify when she should be transitioned to oral therapy. When pediatric infectious disease was consulted, they advised there was no clearly defined fetal benefit to prolonging intravenous therapy. After delivery, they also recommended against empiric antivirals or diagnostics of the infant if he was well-appearing.

Finally, this patient’s presentation was unique given she denied a history of herpes. Her unremarkable gynecologic history made diagnosing her condition initially challenging as it is rare to have herpes present as meningitis. However, she did endorse a history of migraines and noted that they were in similar character to the headache that had prompted her emergency department presentation. Given this history finding, it was suspected that this patient may have Mollaret meningitis, a rare form of recurrent meningitis often attributed to HSV infection. It is rare for Mollaret meningitis to present as meningitis. However, raising the question of whether her previous migraine was a self-limiting episode of meningitis. Further corroborating this claim is the fact that the majority of Mollaret meningitis patients deny a history of genital herpes [4].
Headaches are a common chief complaint obstetricians manage in their practice. Although rare, HSV meningitis should be considered in the differential diagnosis for patients complaining of a persistent headache. In addition, when treating patients with atypical presentations, a multidisciplinary approach should be encouraged in order to make a timely diagnosis and treatment plan.

Contributors

David Boedeker was the primary author and resident who cared for this patient during her antepartum and postpartum course.

Angela Shaddeau oversaw this patient’s care as the maternal-fetal medicine attending, and added to the case report the unique perspective of a high-risk obstetrician.

Both authors approved the final manuscript.

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