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Disseminated primary herpes simplex infection imitating preterm prelabor rupture of membranes – a case report

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ABSTRACT

Background: We describe a case of primary herpes simplex virus (HSV) infection imitating preterm prelabor rupture of membranes (PPROM) and review the intricacies of establishing the diagnosis.
Case presentation: At 18 weeks of gestation, a patient was referred for suspected PPROM following leakage of fluid and a positive nitrazine test. The patient had a swollen inguinal lymph node, intermittent fevers, transaminitis, labial lesions, and cervical ulceration with vaginal discharge. Amniotic fluid volume was normal. An HSV PCR test was positive. Intravenous acyclovir followed by oral valacyclovir resulted in resolution of symptoms.
Conclusion: Discharge from HSV cervicitis can present as nitrazine-positive pooling, imitating PPROM. A high index of suspicion is warranted, especially when the amniotic fluid volume is normal and arborization is not seen on microscopic exam.

1. Introduction

Accurately diagnosing preterm prelabor rupture of membranes (PPROM) is crucial. At least 50% of women with PPROM will deliver within one week of membrane rupture. Expedient and accurate diagnosis of PPROM, especially at peri-viable gestational ages, is important to determine the most appropriate interventions [1]. In pre-viable PPROM, the prognosis is poor and expectant management versus induction of labor should be offered to the patient [2]. Various tools and techniques are available to assist in establishing the diagnosis of PPROM, including examination for vaginal pooling, nitrazine pH evaluation, visualization of arborization with a microscope, volume assessment by ultrasound, and amniocentesis with infusion of indigo carmine. Additionally, there are commercially available laboratory tests which detect PAMG-1, IGFBP-1, placental protein 12, alpha-fetoprotein, and/or fetal fibronectin.

Each test has limitations; therefore multiple techniques may be used in combination. Nitrazine is a pH test and has been documented to have a specificity between 16% and 70% [3]. Physiologic vaginal secretions have a pH of 4.5–6.0 whereas amniotic fluid is 7.1–7.3. Blood, sperm, lubricant jelly, discharge, and bacterial vaginosis can all cause a positive result. Pooling is traditionally a more specific physical exam finding suggestive of ruptured membranes (70–88%) [3]. Ferning may be falsely negative if the slide does not have sufficient time to dry or the sample was inadequate. A false positive can occur when cervical mucous ferns. When conflicting results arise and clinical doubt remains, establishing the correct diagnosis can be challenging. Further observation and repeat examinations are warranted in such cases. We present a case where a diagnosis of PPROM was strongly suspected after initial exam due to pooling of a large amount of nitrazine-positive fluid. However, after careful consideration of the patient's history and finding other symptoms of infection with repeated assessments, an alternative diagnosis of primary HSV was established.

2. Case Presentation

A 23-year-old woman (gravida 2, para 0, abortus 1) at 18 weeks and 1 day of gestation, with no remarkable medical history, was referred to labor and delivery for further evaluation of suspected PPROM. Four days prior, the patient presented to the emergency department with left-sided groin pain. She was found to have a white blood cell count of 14×10^9/L, elevated AST of 58 U/L and ALT of 68 U/L, with otherwise normal laboratory evaluation. She was diagnosed with a groin strain and discharged to home.

She returned two days later with general malaise and weakness. Vital signs were significant for a temperature of 39.1 °C and maternal heart rate of 129 beats per minute. Laboratory evaluation demonstrated a white blood cell count of 7×10^9/L but further elevated AST of 72 U/L

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and ALT of 106 U/L. Coronavirus-19 testing was negative. The fever resolved with fluid resuscitation and an obstetric ultrasound scan was reassuring, so the patient was discharged. Soon after, the patient experienced leakage of clear vaginal fluid. A pelvic examination was performed in the office and a considerable amount of pooling of nitrazine-positive vaginal fluid was seen; a ferning test and ultrasound were not performed at that time. The patient was sent to the hospital for further evaluation given suspected PPROM.

Upon presentation to labor and delivery, vital signs were within normal limits and no tenderness was noted on abdominal exam. A tender and enlarged lymph node was noted in the left inguinal area. Repeat pelvic examination confirmed the previous findings: there was a large amount of thin, straw-colored, nitrazine-positive fluid pooling in the posterior vaginal vault. However, it was also noted that the distal aspect of the cervix was inflamed and friable. A shallow, ulcerative lesion approximately 1 cm in size with a pale base and raised, erythematous borders overlayed on tissue with a blue hue was identified at approximately 11 o'clock on the cervix. Externally, a 1 cm ulcerated lesion was seen along the left labia and two vesicles on erythematous bases were seen on the posterior fourchette. Microscopic evaluation of the vaginal fluid was negative for ferning. This exam was repeated after two hours of ambulating with a perineal pad in place and it was unchanged. The patient was counseled on the possibility of PPROM, though the diagnosis of primary HSV infection was considered, given normal amniotic volume measurements, negative fern testing, and lesions on pelvic exam. An amnio-dye instillation test was declined by the patient in favor of expectant management. Commercially available diagnostic tests were not available locally. A sample of vaginal fluid was taken as the patient did not tolerate unroofing of the cervical or labial lesions. This was sent for HSV-PCR and a Tzanck smear.

Laboratory evaluation was significant only for worsening transaminitis, with AST 277 U/L and ALT 259 U/L, and a normal white blood cell count. Considering the transaminitis and fever, testing for hepatitis, cytomegalovirus, Epstein-Barr virus, syphilis, and human immunodeficiency virus were performed as well as an abdominal ultrasound scan, which were all normal. The patient had documented negative HSV-1 and HSV-2 serology in the first trimester and therefore serological immunoglobulin testing was repeated to compare. The patient was admitted in anticipation of a repeat exam after 24 h of monitoring. Overnight the patient became febrile (maximum temperature of 39.1 °C). Given suspicion for disseminated HSV infection, intravenous acyclovir was started. Repeat laboratory studies showed a persistent transaminitis, with AST 225 U/L and ALT 222 U/L, and a normal white blood cell count, and infectious disease was also consulted.

Repeat pelvic examination the following day was unchanged. Tzanck smear was negative; however, the HSV-PCR returned positive for HSV-2 48 h later. The patient improved with acyclovir: the amount of vaginal fluid began to decrease and the transaminitis improved. Shortly thereafter the serological testing returned with positive IgM for HSV-2. Prior to discharge, the patient was transitioned to oral valacyclovir twice a day for a total of 10 days. Five months later, the patient presented to another outside facility with spontaneous rupture of membranes at 39 weeks and 2 days and delivered vaginally. The authors have not had access to the records on fetal outcome.

3. Discussion

PPROM is associated with severe morbidity and mortality. Establishing the correct diagnosis is extremely important, especially in the peri-viable period. In this case, what was thought to be pooling amniotic fluid was instead a copious amount of straw-colored, alkaline discharge from a cervical HSV lesion. Given the absence of ferning and normal amniotic fluid volumes, the managing team maintained a high index of suspicion for alternative etiologies. Utilization of multiple techniques to diagnose PPROM was necessary to establish the correct diagnosis.

Cordeiro et al. reported a similar case of HSV presenting as PPROM [4]. The authors had similar initial findings; however, they reported presumed amniotic fluid ferning. They described a cervix with multiple white plaques against a blue stromal background and initially there was concern for malignancy. A diagnosis of HSV was made when cellular changes consistent with HSV were evident on a Pap smear.

Primary HSV infections occur in about 2% of pregnancies [5]. Neonatal mortality from HSV has decreased but is still 30% for disseminated disease and 4% for central nervous system disease. Approximately 20% of those who survive will have long-term neurologic symptoms [6]. Our patient had active labial lesions; these can be unroofed and the contents sent for viral culture or PCR. If there are no lesions, antibody testing can be used and will become positive within the first few weeks of infection and persist indefinitely [7]. Intravenous acyclovir is indicated for patients with findings of disseminated HSV; empiric treatment can be started while awaiting confirmatory results. The cumulative findings of an enlarged lymph node, cervical ulceration, discharge, fever, and transaminitis were inconsistent with PPROM and explained only by a primary HSV infection, which was confirmed with diagnostic testing [8,9].

In this case, the presentation of HSV cervicitis was similar to that of PPROM. A diagnosis of PPROM at this pre-viable gestational age has a poor prognosis and could have resulted in an inappropriate termination of the pregnancy. Fever made the diagnosis more challenging and of critical importance because chorioamnionitis would have also indicated the need for delivery. After collecting a thorough history and physical exam, a diagnosis of primary, disseminated HSV became more apparent. Empiric treatment was started and further testing confirmed the diagnosis. As we maintained a high suspicion for alternative diagnoses, our counseling in the pre-viable period was eventually more reassuring for a positive outcome. It is important to review the strengths and weaknesses of each of the methods used in the diagnosis of ruptured membranes and maintain a high index of suspicion for alternative etiologies, including HSV.

Contributors

Dylan Campbell contributed to patient care, conception of the case report, acquiring and interpreting data, drafting the manuscript, undertaking the literature review and revising the article critically for important intellectual content.

Henry Lesser contributed to patient care, conception of the case report, and revising the article critically for important intellectual content.

Robert M. Ehsanipoor contributed to patient care, undertaking the literature review, and revising the article critically for important intellectual content.

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Patient consent

The patient provided consent for her case to be published with identifying information removed. She did not consent to images being taken of her exam findings so none have been included in this report.

Provenance and peer review

This article was not commissioned and was peer reviewed.

Conflict of interest statement

The authors declare that they have no conflict of interest regarding the publication of this case report.

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