Preterm Premature Rupture of Membranes at 27 Weeks Gestation with Vaginal Colonisation by *Haemophilus influenzae*: A Case Report

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Abstract:

Preterm premature rupture of membranes (PPROM) is a significant contributor to preterm births and is associated with increased maternal and neonatal morbidity and mortality. Early identification and appropriate management are crucial to prolong gestation and minimise complications. We report a case of PPROM at 27 weeks of gestation complicated by vaginal colonisation with *Haemophilus influenzae,* highlighting the importance of microbiological evaluation in such scenarios.

Key words: Preterm Premature Rupture of Membranes, *Haemophilus influenzae*, Preterm Birth, Antenatal Infection, Neonatal Sepsis.

Introduction

A high vaginal swab (HVS) culture during preterm labour is important as it identifies infections that can induce preterm labour or lead to complications in the newborn or the mother, enabling targeted antibiotic therapy to improve outcomes. It helps in the diagnosis of bacterial vaginosis and chorioamnionitis, both of which are strongly associated with preterm labour and severe neonatal complications such as sepsis.[1]

Several pathogens have been implicated in preterm labour, among which *Haemophilus influenzae (H. influenzae)* is a lesser-known but important organism. Although typically a respiratory commensal, *H. influenzae* can colonise the female genital tract[2] and cause infections such as pelvic inflammatory disease and vulvovaginitis. During pregnancy, it has been associated with miscarriage, intra-amniotic infection, preterm childbirth, and, in severe cases, systemic infections such as sepsis or bacteraemia. Notably, strains isolated from the genital tract are usually non-typeable *H. influenzae* (NTHi), which have a recognised ability to cause invasive maternal and neonatal disease.[1] We have highlighted here a clinical case of preterm labour where *H. influenzae* was isolated from the HVS.

Case Report

A 28-year-old woman, gravida 2, para 1, live 1 (G2P1L1), presented at 27 weeks of gestation with complaints of leaking per vaginum since the morning. She denied any associated pain, fever, vaginal bleeding, or uterine tenderness. On examination, the patient was found to be stable, afebrile, and normotensive. On per-abdominal examination, the uterus was found to be relaxed, with no signs of tenderness or contractions. Per speculum examination showed clear fluid leaking per vaginum; digital per vaginal examination was deferred to avoid ascending infection. On ultrasound examination, a single

live intrauterine pregnancy at 27 weeks, with a reduced amniotic fluid index, was noted. An HVS was sent for culture, which showed growth of *H. influenzae*. The isolate was sensitive to azithromycin, ciprofloxacin, and levofloxacin, but resistant to amoxycillin-clavulanic acid, ampicillin-sulbactam, ampicillin, cefuroxime, cefixime, ceftriaxone, and co-trimoxazole. All other tests were within normal limits; there was no leukocytosis or elevated C-reactive protein.

The patient was admitted for inpatient monitoring and started on azithromycin tailored to culture sensitivity. Antenatal corticosteroids (betamethasone 12 mg intramuscularly, two doses 24 hours apart) for foetal lung maturity were given, along with magnesium sulphate for neuroprotection, considering the risk of imminent preterm birth. Serial monitoring of maternal vitals, signs of infection, and foetal wellbeing was done. The pregnancy was conservatively managed with close surveillance. No signs of chorioamnionitis or foetal compromise were observed during the initial 72 hours. The patient remained stable and was managed expectantly to prolong gestation. Neonatal and infectious disease teams were involved in planning neonatal care and potential sepsis screening post-delivery.

Discussion

Preterm premature rupture of membranes (PPROM) refers to the rupture of foetal membranes before 37 weeks of gestation and prior to the onset of labour. It complicates approximately 2%–3% of all pregnancies and accounts for nearly one-third of preterm deliveries.[3,4] The presence of genitourinary tract infections, including colonisation with atypical organisms such as *H. influenzae*, can increase the risk of ascending infection and adverse neonatal outcomes.[5]

H. influenzae is an uncommon cause of vaginal colonisation during pregnancy but can be associated with chorioamnionitis, neonatal sepsis, and poor pregnancy outcomes if not promptly identified and treated. PPROM presents a complex clinical scenario, balancing the risks of prematurity against those of infection.[4] Identification of pathogenic organisms via vaginal cultures is vital in guiding appropriate antibiotic therapy and improving perinatal outcomes. In another study, the overall rate of invasive *H. influenzae* infections linked to pregnancy was similar to the incidence of early-onset neonatal sepsis caused by group B *Streptococcus*, and notably higher than the rate of pregnancy-related listeriosis.[5] Pregnant individuals face a 17-fold higher risk of developing invasive *H. influenzae* infections, most commonly due to non-typeable strains. When such infections occur within the first 24 weeks of gestation, they are linked to a foetal loss rate exceeding 90%.[5] Case studies have documented intra-amniotic infections with histological signs of acute necrotising chorioamnionitis, indicating that maternal *H. influenzae* infections can extend into the amniotic cavity and potentially affect the foetus.[6] During pregnancy, changes in hormonal, metabolic, and immune functions that support foetal development may also facilitate the movement of *H. influenzae* from the vaginal area into the uterine cavity, potentially raising the risk of placental infection.[7] Strains of *H. influenzae* linked to maternal infections are frequently associated with ascending infections and tend to show a particular affinity for the genital tract.[4]

Treatment of *H. influenzae* vaginal colonisation in pregnancy primarily involves the use of broad-spectrum antibiotics, with third-generation cephalosporins such as ceftriaxone or cefotaxime commonly recommended due to their proven efficacy against *H. influenzae* and favourable safety profile during pregnancy. In cases of polymicrobial infections, which are frequent in obstetric settings, combination antibiotic therapy may be required. A typical regimen includes ampicillin with gentamicin; however, gentamicin's limited activity against *H. influenzae* and its potential for nephrotoxicity and ototoxicity must be considered. For patients with penicillin allergies, alternative antibiotics such as clindamycin or azithromycin can be used, depending on the susceptibility profile of the isolated strain.[8]

Our isolate was sensitive to macrolides and fluoroquinolones, but resistant to β-lactams and their combinations with β-lactamase inhibitors. β-lactam resistance, including resistance to amoxicillin-clavulanate and ceftriaxone, cannot be explained solely by β-lactamase production, because clavulanic acid (a β-lactamase inhibitor) should restore activity in β-lactamase-producing strains. This isolate is most likely a β-lactamase-negative, ampicillin-resistant (BLNAR) strain. Such strains are known to have mutations in the ftsI gene, which encodes penicillin-binding protein 3 (PBP3). This leads to reduced binding affinity for β-lactams, resistance to ampicillin, amoxicillin-clavulanate, and

some cephalosporins (e.g., ceftriaxone), in the absence of β-lactamase production. These strains are not neutralised by β-lactamase inhibitors like clavulanic acid because the resistance is due to altered PBPs, not enzymatic degradation.[8] Sensitivity to macrolides and fluoroquinolones indicates the absence of efflux pump overexpression or target-site mutations (e.g., in 23S ribosomal ribonucleic acid [rRNA] or deoxyribonucleic acid [DNA] gyrase/topoisomerase genes). Hence, azithromycin and ciprofloxacin remain effective.

This case highlights the importance of thorough microbiological evaluation in cases of PPROM and emphasises individualised management. The use of chocolate agar during microbiological processing can aid the isolation of *H. influenzae*. Additionally, satellitism using a staphylococcal streak on sheep blood agar can facilitate prompt identification. Timely identification and treatment of atypical pathogens such as *H. influenzae* can help reduce maternal and neonatal complications while safely prolonging pregnancy when possible.

Declarations:

This study was not funded by any person or organisation. All authors agree to the content of the manuscript. Patient details have been de-identified and are not mentioned to maintain confidentiality and privacy.

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Conclusion

This case highlights the importance of considering atypical pathogens such as *H. influenzae* in PPROM. Early microbiological identification and susceptibility-guided therapy enabled appropriate management and safe prolongation of pregnancy without maternal or foetal complications. Routine vaginal cultures in PPROM can aid in timely, targeted treatment and may help improve perinatal outcomes.

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