Missed Abortion Caused by H. Influenzae Septicemia in a Saudi Woman; A Case Report

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Abstract:

Hemophilus influenza has been reported to cause miscarriages globally, but no such case has ever been reported from Saudi Arabia. A 25 years old female, pregnant for 10 weeks and 2 days, presented with fever, mild sore throat and shivering in OBGYN outdoor. First blood culture showed positive growth of Hemophilus influenzae, sensitive to Cefepime. Urine culture and high vaginal swab were negative. She was treated with Ceftriaxone, metronidazole, and paracetamol infusion. Ultrasound showed missed abortion at 11 weeks 1 day. Tablet Misoprostol, sublingual, was started to terminate the pregnancy. She expelled the fetus on 13-11-2024, and ultrasound showed that it was an incomplete abortion, hence curettage was done. After curettage, she remained stable and was discharged. A repeat blood culture was taken before discharge, and no growth was observed. “Take-away” lesson is that infection by H. influenzae in early pregnancy should be taken seriously.

Keywords: Hemophilus Influenzae, miscarriage,Saudi Arabia

Introduction:

During pregnancy, women undergoan altered immune response, increasing the risk of infection and sepsis.[1]Hemophilusinfluenzahas been reported to infect pregnant women and cause miscarriages in the USA, UK, Europe, New Zealand, and Japan, [2-6]but no such case has ever been reported in Saudi Arabia. We present a case report of missed abortion in Saudi Arabia following sepsis caused by Hemophilus influenzae.

Case report:

A female patient, 25 years old, was booked in early pregnancy, her dating scan was done on 07-11-2024 and it showed a viable pregnancy of 10 weeks 2 days. She was married for 10 months, and pregnant for 10 weeks and one day according to LMP (last menstrual period). She was taking Xonvea (doxylamine succinate and pyridoxine hydrochloride) for nausea and vomiting during pregnancy. She was also on dydrogesterone, and progesterone as she had a history of abdominal pain. She also gave a history of genital herpes in January 2024 and was treated for that.

Clinical findings: She presented in the ER on 10-11-2024 with a fever and mild sore throat for one day. She was sent home on oral antibiotics and analgesics with follow-up advice. But, on 11-11-2024, she presented in the OBGYN clinic with shivering and fever. She was referred to internal physician as from OBGYN side everything was good. On 12-11-2024, she was admitted under internal physician due to fever with shivering. Her

temperature was 39 ºC and on examination her throat was congested. On the same date, patient was transferred under OBGYN care as she was free from internal medicine according to them. In evening on 12-11-2024, she had severe shivering and temperature spiked till 39 ºC. Along with Ceftriaxone, metronidazole

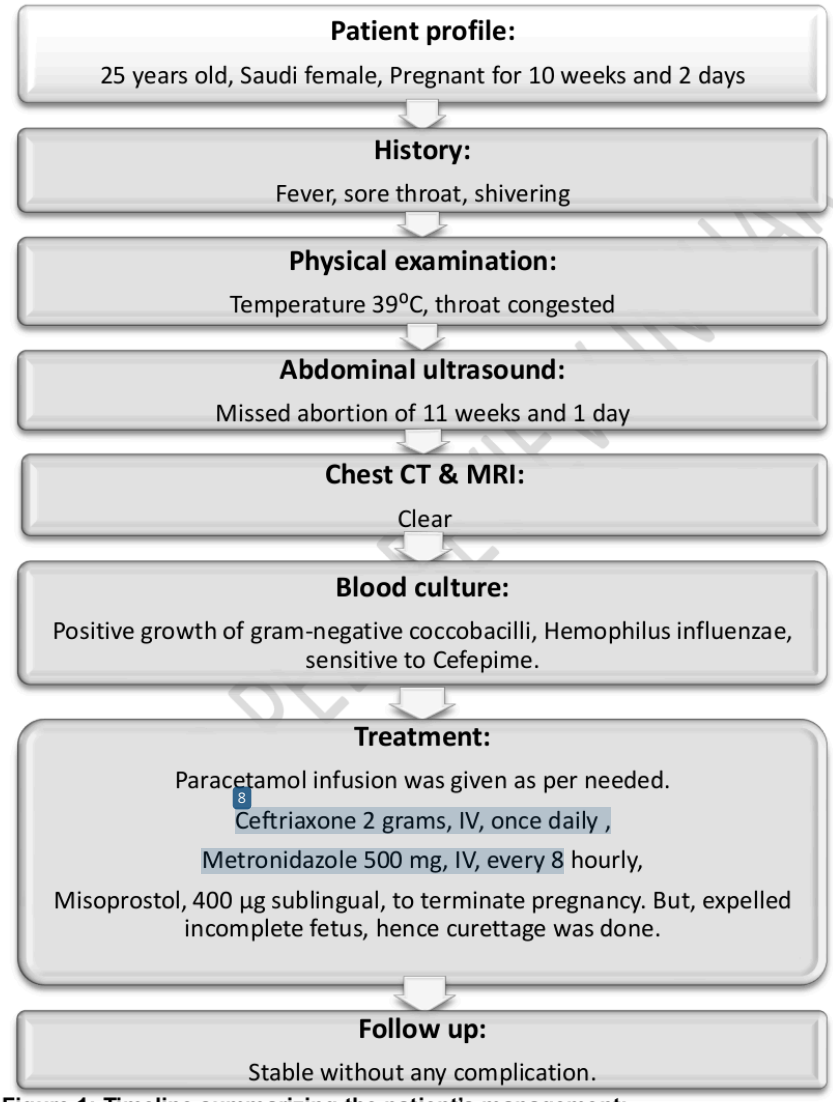

Figure 1: Timeline summarizing the patient's management:

500 mg intravenous every 8 hourly was started on 13-11-2024. She had severe shivering in the morning on 13-11-2024, but her temperature was normal. Paracetamol infusion was restarted and shivering was settled. The patient was under the care of a pulmonologist, infection control consultant, and a psychiatrist, as the patient looked depressed.

Diagnostic assessment: Her ultrasound was repeated after admission for abdomen and pregnancy. Abdominal ultrasound was unremarkable and pregnancy ultrasound showed missed abortion at 11 weeks 1 day. The first blood culture was sent on 11-11-2024 and it showed positive growth of gram-negative coccobacilli, Hemophilus influenzae, sensitive to Cefepime.Serotyping of H. influenzae showed non-typeable Hemophilus influenzae (NTHi). Urine culture and high vaginal swab were negative. Her chest CT scan and MRI were normal. During admission, her screening for Hepatitis B and C, HIV, and reactive plasma reagin (RPR) were normal. Her blood group was AB positive. Her antibody screen was negative. Her hemoglobin level was 11.5 g/dL. White blood count and differential leucocyte count were normal. Random blood sugar was also normal. The Rubella IgG was reactive. C-reactive protein (CRP) was 153 mg/L on 11-11-2024, which later dropped to 145 mg/L on 14-11-2024. Procalcitonin (PCT) was 12.18 ng/mL on 11-11-2024, which dropped to 4.37 ng/mL on 14-11-2024. Histopathology of products of conception was normal, hence no culture and sensitivity test was done. A repeat blood culture was taken before discharge from the hospital, and no growth was observed after 7 days of incubation.

Therapeutic intervention: She was on paracetamol infusion as per needed. She had severe shivering in the morning on 13-11-2024, but her temperature was normal.

Paracetamol infusion was restarted and shivering was settled. The patient was under the care of a pulmonologist, infection control consultant, and a psychiatrist, as the patient looked depressed. Injection Ceftriaxone two grams iv once daily was started in medical unit. Along with Ceftriaxone, metronidazole 500 mg intravenous every 8 hourly was started on 13-11-2025 in OBGYN ward. On 13-11-2024, after she completed antibiotics for 24 hours, Tablet Cytotec (Misoprostol) 400 μg sublingual, was started to terminate the pregnancy. She expelled the fetus on 13-11-2024, and ultrasound showed that it was an incomplete abortion, hence curettage was done. After curettage, she remained stable and was discharged on 16-11-2024 in good condition.

Follow-up and outcomes: She came in OPD for a follow-up on 24-11-2024 and was in good health.

Discussion:

During pregnancy, women undergo physiological changes and an altered immune response, increasing the risk of infection and sepsis.[1] Pregnancy is a balance between tolerance and rejection of the fetus, and an active infection can probably destabilize this balance, resulting in rejection. The bacterium Hemophilus influenzae is a very common pathogen infecting pregnant women and causing miscarriage. However, these cases were only reported from the USA, UK, Europe, New Zealand, and Japan.[2-6] These cases were caused by either Hemophilus influenzae b (Hib) or non-typeable Hemophilus influenzae (NTHi).

The childhood vaccination against Hib eradicated meningitis caused by this bacterium globally. However, the focus shifted to less severe but prevalent infections

caused by unencapsulated variety, non-typeable Hemophilus influenzae.[5] Similarly, in Saudi Arabia, during the pre-vaccine era, Hemophilus meningitis was the leading cause of bacterial meningitis in children under five years of age. However, after the introduction of the Hib vaccine in 1985, the number of children infected with Hemophilus meningitis dropped dramatically.[7] In 2021, only one case of invasive Hib (encephalitis) and one case of invasive Hib (meningitis) were reported.

Miscarriages caused by infection with non-typeable Hemophilus influenzae (NTHi) also started rising recently in the world.[3]Both Hib and non-typeable Hemophilus influenzae were found to be responsible for these miscarriages in many Western countries and Japan. However, in literature, no case of miscarriage was reported in Saudi Arabia, by any serotype of Haemophilus influenzae. Saudi epidemiological surveillance reports mention only meningitis and encephalitis cases caused by Hib, while other invasive cases caused by Hib are never reported.[7]Similarly, we could not find any case of fetal loss due to the infection of the mother by any serotype of Haemophilus influenzae in other Middle Eastern countries.This could probably be explained due to genetic or racial differences. Racial disparities in Hib disease were reported in the pre-Hib vaccine era in USA. The incidence rate was three to four times higher among Black children and five to ten times higher among American Indians as compared to White children. These racial disparities persist in the Hib vaccine era.[8]Individuals identify antigenic epitopes by using the same Ig V genes. V gene variations might result in divergent immune responses, leading to varying disease susceptibility. One such polymorphism is frequently found in a Native American group, Navajos, who have a 10 times higher incidence of Haemophilus influenzae B infection than control population.[9]

In our case report, the patient presented with fever, sore throat and shivering. None of the previous cases in literature presented with upper respiratory tract infection. Most cases presented with fever, with one or more of the symptoms like per vaginal (PV) bleeding, PV discharge, and abdominal pain. In our case report, blood culture was positive for Haemophilusinfluenzae, whereas high vaginal swab (HVS) and urine culture were negative. Histopathology showed normal products of conception. However, the cases in literature mostly showed positive blood cultures as well as positive HVS cultures. H. influenzae was also isolated from the products of conception in most cases. In some cases found in literature, ascending vaginal infection was the most plausible route of transmission of H. Influenzae.[2,3]However, in other cases, although bacteremia was present, but route of transmission of infection to the fetus could not be found.[4]As the prevalence of H. Influenzae in vaginal flora during pregnancy isvery low,[5] oral sexwas another potential route of intra-amniotic infection,asdetected in one case report.[6]In the light of clinical and laboratory findings, our case pointed towards sepsis through upper respiratory tract infection, leading to missed abortion.

This case reveals the importance of the pathogenicity of H. influenzae during pregnancy. The number of reported invasive H. influenzae infections in pregnant women might be underestimated. H. influenzae has been reported to cause septic abortion, hence, these pathogens should be screened during pregnancy. We had a few limitations in our case report. Firstly, culture and sensitivity of products of conception was not done due to insurance issues for the patient. Secondly, due to retrospective nature of the report some information might have been missed.

Primary “take-away” lesson of this case report is that the burden of invasive disease by H. influenzae in early pregnancy loss is much larger than actually considered. H. influenzae infection should be seriously attended in early pregnancy.

Conflict of interest: None

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