

# *Haemophilus influenzae* Sepsis and Placental Abruption in an Unvaccinated Immigrant

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**Background:** *Haemophilus influenzae* infections have declined dramatically in the United States since implementation of the conjugate vaccine. However, in countries where widespread immunization is not routine, *H influenzae* remains a significant cause of morbidity and mortality. We report a case of a previously unvaccinated immigrant with confirmed *H influenzae* sepsis and placental abruption leading to spontaneous abortion.

**Objectives:** To alert emergency medicine practitioners that *H influenzae* should be recognized as a maternal, fetal, and neonatal pathogen. Clinicians should consider this diagnosis in immigrants presenting with uncertain vaccination history, as *H influenzae* can cause significant morbidity and mortality.

**Case Presentation:** A 36-year-old female was referred to our emergency department (ED) with lower abdominal pain with some vaginal spotting. The patient had an initial visit with normal laboratory investigations and normal imaging results, with complete resolution of symptoms. The patient returned to the ED with sudden onset of vaginal bleeding and abdominal pain. She presented at this time with sepsis, which progressed to septic shock, causing placental abruption and ultimately, spontaneous abortion. The patient was treated with pressors and antibiotics and was admitted to the medical intensive care unit where she received ampicillin, gentamycin, and clindamycin for suspected chorioamnionitis. The patient's blood cultures came back positive after 1 day for *H influenzae*. The patient did well and was discharged from the hospital 4 days later.

**Conclusion:** *Haemophilus influenzae* should be recognized as a neonatal and maternal pathogen. Clinicians should consider this diagnosis in immigrants presenting with uncertain vaccination history, especially in pregnant females, as *H influenzae* can cause significant morbidity and mortality. [West J Emerg Med. 2012;13(1):133–135.]

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## INTRODUCTION

*Haemophilus influenzae* infections have declined dramatically in the United States since the conjugate vaccine became available in 1988.<sup>1</sup> However, in countries where widespread immunization is not routine (including Southeast Asia, Africa, the western Pacific, and the eastern Mediterranean), *H influenzae* remains a significant cause of mortality. There were an estimated 8.13 million infections and 371,000 deaths in 2000 alone. Most deaths worldwide are in Africa and Asia; however, infections from nontypable *H*

*influenzae* continue to pose a problem within the United States.<sup>2</sup> Cases of *H influenzae* infections in pregnant females have been documented in case reports, usually resulting in significant maternal and fetal morbidity.<sup>3–8</sup> The incidence of *H influenzae* bacteremia in pregnant females, causing sepsis and eventual spontaneous abortion, has not been well documented in the literature. We report a case of a previously unvaccinated immigrant with confirmed *H influenzae* sepsis and placental abruption, which resulted in a spontaneous abortion.

**CASE REPORT**

The patient was a 36-year-old female, gravida 4, para 3, pregnant at 16 weeks and 1 day (confirmed by previous ultrasonography) who presented to an ambulatory health center with complaints of 1 day of lower abdominal and flank pain with some vaginal spotting. She also endorsed a history of mild dysuria with urinary frequency and urgency at that time. She reported no fever, chills, or sick contacts. She was referred to the emergency department (ED) for further evaluation. She had no past medical history but had arrived in the United States from Pakistan 8 months earlier. Her ED vital signs showed a blood pressure of 103/70 mmHg, a heart rate of 133 beats per minute (bpm), a temperature of 99.9°F, and a respiratory rate of 16 per minute with an oxygen saturation of 99% on room air. The patient was well appearing, and her physical examination was notable for tachycardia, suprapubic tenderness without rebound or guarding, and a pelvic examination with slight bleeding but no uterine tenderness. Her laboratory results showed a leukocytosis of 16.1 K/ $\mu$ L with 88% polymorphonuclear leukocytes, which was considered within the normal range for the second trimester of pregnancy. The remainder of the complete blood count, chemistry panels, and urinalysis were unremarkable. An ultrasonogram of her abdomen showed a live intrauterine pregnancy with an estimated gestational age of 16 weeks and 0 days, with a fetal heart rate of 182 beats per minute. Magnetic resonance imaging (MRI) of the abdomen was interpreted as normal, without evidence of appendicitis. She received 4 liters of normal saline, 2 mg of morphine sulfate, and 975 mg of acetaminophen. Her heart rate improved to 100 bpm and she felt better. She was seen by an obstetrician consultant in the ED and discharged home with obstetrician follow-up and instructions to return with any concerns.

She returned to the ED 1 day later with sudden onset of vaginal bleeding and abdominal pain. Her vital signs were concerning for a heart rate of 139 bpm, a blood pressure of 149/88 mmHg, a respiratory rate of 30 per minute, and oxygen saturation of 100% on room air. Further examination revealed that the patient was actively delivering the products of conception. An obstetrician was emergently consulted and arrived minutes later. They delivered an intact fetus and gestational sac shortly after their arrival. The patient received 800 mg of rectal misoprostol. A tympanic temperature at this time was measured at 105°F. The patient was persistently tachycardic into the 140s. The patient became hemodynamically unstable with a blood pressure of 84/35 mmHg and central intravenous access was obtained. The patient was given acetaminophen, intravenous normal saline, and given vancomycin and piperacillin/tazobactam, with a working diagnosis of sepsis of unknown etiology. Her laboratory results revealed a venous pH of 7.22, an anion gap of 21 with a lactate concentration of 10.8 mmol/L. Her complete blood count at this time showed a white blood cell count of 14.9 K/ $\mu$ L and 85% polymorphonuclear leukocytes. The patient had normal MRI and urinalysis findings and no symptoms to suggest colitis, skin infection, or other soft tissue infections. The patient was given

norepinephrine for persistent hypotension and admitted to the medical intensive care unit where she received ampicillin, gentamycin, and clindamycin for suspected chorioamnionitis. An ultrasonogram was suggestive of retained products of conception and that night the patient underwent dilatation and curettage with removal of tissue debris. The patient did well and was discharged from the hospital 4 days later.

The patient's blood cultures came back positive after 1 day for *H influenzae*, non- $\beta$ -lactamase producing, although further identification of the molecular characteristics of the bacteria, which requires slide agglutination for serotyping or polymerase chain reaction for capsular typing, was not performed. The pathology report showed retroplacental hemorrhage occupying 20% of the placental disc and adjacent infarct, consistent with placental abruption. There was no histologic evidence of acute chorioamnionitis.

**DISCUSSION**

Placental abruption is the separation of a normally implanted placenta due to decidual hemorrhage before delivery of the fetus. The incidence of placental abruption is approximately 1 in 100 births and accounts for 10% to 15% of perinatal mortality.<sup>9–11</sup> Acute placental abruption can cause significant maternal and fetal compromise; the risk to the fetus depends on the severity of the abruption and the gestational age at which the abruption occurs, and the danger to the mother is primarily dependent on the degree of abruption.<sup>9,11</sup> Abruption is associated with a ninefold increased risk for stillbirth.<sup>9</sup> Although there has been significant epidemiologic and clinical research into the causes of placental abruption, the underlying etiology and sequence of events at a molecular level are still not well understood. A number of risk factors for placental abruption have been identified, including maternal age and parity, cigarette smoking, hypertension, preeclampsia, and intrauterine infection.<sup>11</sup> The role of nonintrauterine maternal infection is less clear, but there is circumstantial and animal-model evidence to suggest that it is implicated in at least a portion of preterm pregnancy complications, and intrapartum fever has been found to be associated with increased risk of placental abruption as well.<sup>12,13</sup> Given the lack of other risk factors for placental abruption and the temporal relationship of the patient's sepsis and abruption, it is likely that sepsis secondary to an acute *H influenzae* infection led to placental abruption and ultimately, spontaneous abortion.

*Haemophilus influenzae*, primarily serotype B, causes serious invasive diseases, usually in children younger than 5 years.<sup>14</sup> Hib conjugate vaccines were first licensed for children in the United States in 1988, with subsequent licensure in 1990. Since implementation, the number of reported Hib invasive disease cases among children younger than 5 years has declined 99%.<sup>1</sup> Nontypable *H influenzae* is distinguished from the serotyped strains by the absence of a polysaccharide capsule. Nontypable strains cause invasive disease in children less frequently than encapsulated *H influenzae*, but are increasingly recognized as pathogens in adults, particularly for the

immunocompromised person.<sup>15,16</sup> Nontypable *H influenzae*, (particularly biotype 4) can colonize the genital tract of women. It can cause significant neonatal disease, including sepsis and pneumonia, owing to vertical transmission, as well as postpartum maternal sepsis with endometritis, tuboovarian abscess, and chronic salpingitis.<sup>17</sup> There is a sixfold increased risk for *H influenzae* bacteremia in pregnant women aged 18 to 39 years compared with other adults of the same age. Over half of the pregnancies associated with bacteremia in 1 prospective study resulted in fetal death, and a retrospective study found that 65% of fetuses were infected if mothers were, with a mortality rate of 44% in fetuses that were infected.<sup>15,4</sup>

Emergency physicians are frequently required to treat infections before the specific bacterial pathogen is identified. Maternal/fetal sepsis of unclear etiology ought to initially be treated with broad-spectrum antibiotics to empirically cover likely potential infective agents. When diagnostic testing has confirmed infection is due to *H influenzae*, treatment can be tailored to this specific organism.  $\beta$ -Lactam antibiotics, such as amoxicillin, have generally been considered first-line agents against *H influenzae*, although there have been reports both in the United States and worldwide of significant  $\beta$ -lactamase resistance including resistance to amoxicillin-clavulonate,<sup>18,19</sup> requiring a second- or third-generation cephalosporin. Alternative choices of antibiotics with activity against *H influenzae* include macrolides, aminoglycosides, fluoroquinolones, and tetracyclines.

## CONCLUSION

Although the epidemiology of *H influenzae* is changing both in the United States as well as worldwide, owing to the Hib vaccine, there is still significant morbidity from this illness.<sup>16,20</sup> The illness described in our patient exemplifies how *H influenzae* should be recognized as a maternal, fetal, and neonatal pathogen. Clinicians should consider this diagnosis in immigrants presenting with uncertain vaccination history, especially in pregnant females, as *H influenzae* can cause significant morbidity and mortality.

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*Conflicts of Interest:* By the WestJEM article submission agreement, all authors are required to disclose all affiliations, funding, sources, and financial or management relationships that could be perceived as potential sources of bias. The authors disclosed none.

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