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Case Report

Salmonella Bacteremia in the Second Trimester: A Case Report -

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ABSTRACT

Millions of Americans are still affected by different *Salmonella* serotypes annually, but the adverse events related to the infection are relatively uncommon. Salmonellosis has been reported in multiple cases as a cause for spontaneous abortion, yet, it is unclear how exactly *salmonella* bacteremia affects the unborn fetus. The Th1/Th2 cytokine theory is one of the proposed mechanisms. A 38 year old, 12 weeks pregnant, female was admitted to a family medicine service with *salmonella* bacteremia, after multiple emergency department presentations, and ultimately experienced a spontaneous abortion. This case proposes that pregnant women with persistent abdominal and diarrheal symptoms be tested for *Salmonella*.

Keywords: *Salmonella*; Bacteremia; Abortion

INTRODUCTION

Salmonellosis during pregnancy is extremely dangerous, not only for the life of the expectant mother, but can also cause significant harm to the stable development of the fetus. The placenta is a metabolically active organ which inadvertently supports the proliferation of bacteria, which in some cases is detrimental to the fetus. This cascade allows for apoptosis of placental tissue and localized inflammatory reactions [1-3]. Healthy adults are not routinely screened for *Salmonella* when they present with diarrheal illness, as most people are able to clear it. Therefore, previously healthy pregnant women tend not to be screened either. The current proposed theories of salmonellosis effects on the placenta are somewhat dated. However, there is evidence that vertical transmission of *salmonella* is a distinct possibility [4]. We present a case of a pregnant 38 year old who experienced a spontaneous abortion after weeks of *Salmonella* induced gastrointestinal symptoms.

THE CASE

A twelve week pregnant 38 year old G5P3013 female, who stopped smoking marijuana when she learned she was pregnant, had a new two month old thigh size tattoo, a history of trichomonas this pregnancy, and who had not yet established care with an obstetrician was admitted to a family medicine service after multiple emergency department visits within the previous 3 months. Eleven weeks prior to admission she presented with abdominal pain, nausea, vomiting, and non-bloody diarrhea and was diagnosed with gastroenteritis, after eating a fast food burger. She continued to have abdominal pain and vomiting for some time and later developed hematemesis. She was treated for worsening chronic gastroesophageal reflux. Four weeks later she was noted to be six weeks and three days pregnant with a bicornuate uterus, on ultrasound. She later presented with a fever of 38.8°C, body aches, chills, and a headache which was treated as a viral etiology, with supportive measures, and diagnosed with a migraine. Her liver enzymes were noted to be elevated to AST 53 U/L (ref 13-39) and ALT 56 U/L (ref 7-52) at that time. Due to continued vomiting and was diagnosed with hyperemesis gravidarum. Eight and a half weeks after initial presentation she was admitted to the obstetric service with intractable vomiting, non-bloody diarrhea, and abdominal pain with a further rise in her AST to 71 U/L and her ALT to 128 U/L. It was believed that this acute increase in emesis was due to a new type of sausage she had eaten, however no one else in her family was sick. During this admission she was noted to be persistently hypertensive and started on Nifedipine and Aspirin for Preeclampsia prevention. Five days later, now twelve weeks pregnant, she represented to the ED with a fever of 39.5°C and a headache. Blood cultures were drawn and labs were collected, which revealed a normalization in her liver enzymes, and she was treated with a dose of Tamiflu, for presumptive influenza. However, that same day she was

called back to the hospital due to her blood cultures being positive for gram negative rods.

She continued to be febrile at the time of admission to 39.6°C with a blood pressure of 114/57 mmHg and heart rate of 118 bpm. She denied any abdominal pain, nausea or diarrhea, and had a good appetite. Her physical exam was unremarkable with an appropriately enlarged uterus and abdomen non tender to palpation, without guarding, and normoactive bowel sounds. A bedside fetal heart tracing was obtained with a fetal heart rate of 165 bpm.

DIAGNOSTICS AND ASSESSMENT

Labs were notable for a normal white blood cell count of 11.7 (10E3/mcl (ref 4-10)), anemia (Hb 8.3gm/dL (ref 11.4-14.4)), a lactate level of 2.1 mmol/L (ref 0.5-2.2), and normal ALT and AST. Her urinalysis was normal making pyelonephritis less likely. A chest X-ray revealed some concern for pulmonary edema, however, no concern for pneumonia or intra thoracic infectious process. A lumbar puncture was not done as the patient was clinically stable with no neurological deficits, and negative Kernig's and Brudzinski on exam. Pelvic inflammatory disease was considered; however, her Gonorrhea, Chlamydia, and Syphilis testing was negative.

She was started on Intravenous (IV) Ceftazidime, for broad spectrum coverage, in the emergency department, and later switched to IV Ceftriaxone. Blood cultures at 48 hours were positive for *Salmonella* Sandiego, which was susceptible to Ceftriaxone, therefore a long-term plan for a PICC line and IV Ceftriaxone was set up. However, on day 2 of hospitalization, no fetal heart tones were heard on bedside fetal heart tracing. The obstetrics team was consulted for an official transvaginal ultrasound which revealed a 12 week 3 day fetus without any fetal heart tones and the patient was given the diagnosis of missed abortion.

Due to there no longer being a concern for fetal toxicity, antibiotics were switched to oral Levofloxacin for six weeks.

DISCUSSION

Although it is not completely understood how *Salmonella* bacteremia affects the unborn fetus, it has been reported in multiple case studies [2,4,5]. *Salmonella* bacteremia causing spontaneous abortion is well known amongst veterinarians [5], however it is not commonly high on the differential amongst human patients, especially considering that healthy patients with diarrheal illness are not routinely screened for *Salmonella*. Prevalence in pregnant women is similarly low. Citernes, et al showed that prevalence of *Salmonella* in stool samples of pregnant women at 36 weeks gestational age was shown to be around 0.27%, but in women with diarrhea the prevalence rose to around 3% [6]. Roberts, et al showed that at time of delivery, screening by rectal swab of maternity patients showed 0.2%

Table 1: Relevant lab values.

Gestational Age	6w3d	11w2d	12w
WBC [10 E3/mcL] (ref 4-10)	5.8	12	11.7
Hemoglobin [gm/dL] (ref 11.4-14.4)	10.5	10.8	8.3
Hematocrit [%] (ref 33.3-41.4)	30.7	31.6	25
lactic acid [mmol/L] (ref 0.5-2.2)			2.1
Blood Urea Nitrogen [mg/dL] (ref 7-25)	5	9	7
Creatinine [mg/dL] (ref 0.6-1.2)	0.45	0.5	0.55
AST [U/L] (ref 13-39)	53	71	37
ALT [U/L] (ref 7-52)	56	128	40
ALP [unit/L] (ref 34-104)	64	80	95
beta Human Chorionic Gonadotropin [mIU/mL]	139,530		
Urinalysis			Negative
Blood Cultures			Salmonella Sandiego

Table 2: Salmonella sandiego antibiotic sensitivities.

Drug	Salmonella Species	In terp
Ampicillin		Susceptible
Ceftriaxone	Susceptible	
Levofloxacin	Susceptible	
Trimethoprim/Sulfa	Susceptible	

Salmonella, and 12% of the babies of mothers who were positive also excreted *Salmonella* [7].

We are not necessarily concerned about *Salmonella* in countries where *Salmonella Typhi* is not endemic. However, there are other serotypes of *salmonella* that affect 1.35 million Americans annually, causing severe abdominal cramps, diarrhea, and fevers. There is a high chance of transplacental transmission of non *Typhoidal Salmonellosis* [8].

It is well known that hormone production during pregnancy decreases cell mediated immune function [1], putting pregnant woman at a higher risk of contracting *salmonella* septicemia, chorioamnionitis, and listeriosis [2]. The Th1/th2 cytokine theory has been proposed relating to *salmonella* in pregnancy. During pregnancy the maternal immune system must not reject paternal antigens, however, still needs to protect itself against foreign pathogens. It does this by altering the Th1/Th2 cytokine ratio. Th1 cytokine production is suppressed while increasing Th2 cytokine production in order to protect the fetus from rejection. This now makes the maternal system more susceptible to diseases such as malaria, toxoplasmosis, and *salmonella* for which host immunity is Th1 dependent [2]. The placenta is a metabolically active organ therefore it will inherently support the proliferation of any bacteria that has access to it. The unopposed growth of the bacteria in turn causes a massive inflammatory reaction [3] and apoptosis of placental tissue [2].

Perry, et al utilized an ex vivo floating human placental explant model to demonstrate that the syncytiotrophoblast layer of placenta, which forms around floating and anchoring villi, directly contacting maternal blood, thus acting as a barrier to infection, is invaded by *Salmonella Typhimurium*, however, does not proliferate [9].

Other routes by which blood borne pathogens may infect the

placenta include infection of invasive extravillous trophoblast cells (which form on anchoring villi and remodel the uterine arteries to direct blood flow into the uterus, coming into direct contact with maternal blood), and migration of immune cells that were infected at other sites.

The basis for *Salmonella* induced complications such as miscarriage remain to be identified. *Salmonella* expresses pathogen-associated molecular patterns that induce inflammatory responses. The resulting upregulation of cytokines, such as TNF-alpha, can be associated with pregnancy complications including placental damage [9].

In a case by Coughling, et al. [4] of a 34 year old who had a miscarriage at 16 weeks gestation, gram negative bacilli between the fibrins between the villi of the placenta were identified, which supports the conclusion that *salmonella* crosses into the placenta.

CONCLUSION

There were many factors involved in this case, including poor medical literacy, unhealthy social behaviours, and an unclear source of infection making it unclear if *salmonella* bacteremia was the conclusive cause of our patients second trimester abortion. The lack of placental or uterine swabs for *Salmonella* also limits this conclusion. It is, however, our leading differential. Vertical transmission of *salmonella* during pregnancy is a distinct possibility [1] and can lead to detrimental outcomes. Screening pregnant woman, with multiple presentations due to abdominal pain, vomiting, and diarrhea, as in our case, for *salmonella* should, therefore, be included in their abdominal pain work up.

CONTRIBUTORS STATEMENT

Dr. Mooney conceptualized the report, gathered information, drafted the initial manuscript, and reviewed and revised the manuscript.

Dr. Jo coordinated and supervised the information acquisition, assisted with analysis, and critically reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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