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CASE REPORT

Maternal Septic Shock and Fetal Demise Due to *Bacillus cereus* Infection Following Mid-Trimester Genetic Amniocentesis

Yasong Xu[1,*], Yizhen Ji[1,*], Liangkai Zheng[2,*], Ling Chen[3], Li Sun[1], Qichang Wu[1]

[1]Center of Prenatal Diagnosis, Women and Children's Hospital, School of Medicine, Xiamen University, Xiamen, Fujian, 361000, People's Republic of China; [2]Department of Pathology, Women and Children's Hospital, School of Medicine, Xiamen University, Xiamen, Fujian, 361000, People's Republic of China; [3]Department of Clinical Laboratory, Women and Children's Hospital, School of Medicine, Xiamen University, Xiamen, Fujian, 361000, People's Republic of China

*These authors contributed equally to this work

Correspondence: Qichang Wu, Center of Prenatal Diagnosis, Women and Children's Hospital, School of Medicine, Xiamen University, Xiamen, Fujian, 361000, People's Republic of China, Email qichang_wu@163.com

Background: The ubiquitous *Bacillus cereus* bacterium can cause numerous clinical diseases, from transient bacteremia to life-threatening systemic infections. Studies have indicated that non-anthracis *Bacillus* species, such as *Bacillus cereus*, may be clinically significant concerning placental infection, and the resulting outcomes for the fetus.

Case Presentation: We report a woman who developed an acute intrauterine infection following mid-trimester genetic amniocentesis. Twenty-seven hours after the procedure, the mother experienced septic shock, disseminated intravascular coagulation (DIC), and fetal death. Microbiology cultures of placental and fetal swab samples taken during hysterotomy and maternal blood samples taken upon admission revealed the growth of *Bacillus cereus*. The placental pathological examination revealed a large number of microorganisms in the fetal vessels of the chorionic villi, along with signs of acute villitis and chorioamnionitis.

Conclusion: This case study highlights the significance of placental intravascular organisms in acute intrauterine infection caused by *Bacillus cereus*. It also emphasizes the importance of histological analysis, which offers crucial details about the time of onset of the infection and the causative agents and informs present and future obstetric care of these patients, and the significance of placental intravascular organisms in acute intrauterine infection caused by *Bacillus cereus*.

Keywords: chorioamnionitis, villitis, fetal intravascular organisms, amniocentesis, *Bacillus cereus*, sepsis

Introduction

Amniocentesis is a vital prenatal procedure conducted to diagnose a variety of fetal disorders. Though crucial, amniocentesis can result in the development of a life-threatening maternal septic shock and disseminated intravascular coagulation (DIC). However, with an incidence of only 0.03–0.19%, maternal septic shock and DIC after amniocentesis are comparatively uncommon conditions.[1] Acute intrauterine infection is the most frequent contributor to maternal sepsis and the second-highest cause of pregnancy-related mortality. Acute chorioamnionitis, acute villitis, funisitis, and chorionic vasculitis are examples of acute inflammatory lesions of the placenta brought on by a host reaction to a chemotactic gradient in the amniotic cavity and can occur in the mother or the fetus.[2]

Acute chorioamnionitis typically results from an ascending infection, while acute villitis caused by congenital infections is strongly correlated to fetal sepsis.[3] Reports have indicated the existence of bacteria in the fetal capillaries of the chorionic villi along with a markedly less frequent variation of the acute villitis pattern. This is a considerable consequence of congenital infection that can have detrimental implications for both the mother and the fetus.[4] The most frequent causative organism associated with this rare occurrence continues to be Escherichia coli,[5] however, some even rarer cases of this inflammatory response in the placenta are caused by *Bacillus cereus*. In general, non-

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intestinal infections caused by *Bacillus cereus* are uncommon, however, it is becoming widely acknowledged that *Bacillus cereus* can cause infections in humans. For example, there have been numerous reports regarding the presence of *Bacillus cereus* in preterm infants,[6] patients with hematologic malignancy,[7] and cases of prosthetic valve endocarditis.[8] One case report involving *Bacillus cereus* and severe intraamniotic and placental infections associated with invasive procedures has been reported.[9] In this instance, we report a case involving mid-trimester genetic amniocentesis resulting in maternal septic shock and fetal demise from *Bacillus cereus* infection. During the placental pathological examination, there were numerous microorganisms in the fetal vessels of the chorionic villi, indicating acute villitis and chorioamnionitis.

Case Presentation

Clinical History

An amniocentesis was performed on a 33-year-old G2P1 woman at 17 weeks after a non-invasive prenatal screening test found microdeletions on chromosome 22. The woman had a smooth first pregnancy and a full-term singleton delivered via cesarean section; she had no notable past medical history or drug use. After the procedure, the mother experienced acute fever, vaginal spotting, and abdominal pain 27 hours later. During examination, she had a fever of 39.7°C, tachycardia (heart rate of 120 beats per minute), and a blood pressure of 90/42 mmHg. She was examined using ultrasonography which showed the lack of fetal movement or heartbeat. During admission, she was diagnosed with sepsis, intrauterine fetal demise, and suspected chorioamnionitis. Antibiotic therapy was begun with intravenous moxifloxacin hydrochloride sodium chloride injection (0.4 g every 24 hours). Leukocytosis (white blood cell count: 18,000/mm^3, neutrophil ratio: 89.8%) and thrombocytopenia (platelet count: 57,000/mm^3) were detected in the complete blood count upon admission. Blood chemistry analysis indicated that venous lactate levels (>6 mmol/L) were substantially elevated and liver enzymes were only slightly raised. Interleukin 6 inflammatory markers were increased considerably (>5000 pg/mL), while procalcitonin and C-reactive protein levels only slightly increased. The coagulation profiles revealed elevated levels of d-dimer and fibrin degradation products, low levels of fibrinogen, and a prolongation of the prothrombin time and activated partial thrombin time. Thus, we determined that the patient had an intrauterine infection that resulted in septic shock and DIC, which the amniocentesis may have exacerbated. An urgent hysterotomy under general anesthesia was carried out after the decision to speed up delivery was made. The placenta was submitted for histopathologic analysis, and in the delivery room, fetal and placental swabs were taken. Due to resistance, a higher dosage of antibiotics was changed to meropenem and moxifloxacin. During the procedure, the patient was given 4 g of human fibrinogen, 10 units of cryoprecipitate, 10 units of fresh frozen plasma, and 4 units of packed red blood cells. She continued to be hemodynamically unstable, requiring strong vasopressor dosage and ventilation support. It was observed that the uterus maintained its tone and contracted correctly. An estimated 1000 mL of blood was lost during the procedure, and the patient was also given an extra 2000 mL of crystalloid solution. The patient had hypotension of uncertain etiology (either from excessive blood loss or symptomatic anemia); therefore, the patient was given IV phenylephrine during and following the procedure for further blood pressure support. After the procedure, she was admitted to the surgical intensive care unit (ICU) for additional stabilization and treatment. The patient's signs of multi-organ failure persisted by the second day following the hysterotomy. Acute pulmonary edema and moderate pleural effusion were discovered on an urgent chest computed tomography scan. B natriuretic peptide (BNP), a marker of acute heart failure, increased markedly, and the level of inflammatory markers was continuously elevated. Both the placental and fetal swabs taken during the hysterotomy procedure and the maternal blood taken at admission revealed the growth of Gram-positive bacilli that were subsequently determined to be *Bacillus cereus*. Intravenous vancomycin was included to the treatment regimen in light of the patient's deteriorating condition and the results from the microbiology test. The mother gradually improved. After 2 days, she was taken out of intensive care, given a seven-day antibiotic course, and allowed to go home. Over the ensuing weeks, she continued to recover. This case was approved for publication by the Human Research Ethics Committee of Women and Children's Hospital, Xiamen University (approval number: KY-2022-007-H01). Written informed consent from the patient was obtained for this study.

Microscopic Pathology

Acute chorioamniotic inflammation (Stage 1: Subchoriopleural inflammation) (Grade 1: moderate) was discovered during pathological examination of the placenta (Figure 1). Acute villitis with abundant of microorganisms in the fetal vessels of the chorionic villi were revealed, in the setting of acute diffuse villous inflammation and intervillous inflammation (Figure 2).

Microbiology Testing

Using an automated blood culture device (BD Company of the United States), maternal blood was cultured in a blood culture bottle (Bidi Medical Equipment Co., LTD.). Following an automated system's positive report, the bacteria were examined under a microscope using the BASO Gram staining solution rapid method. The bacteria were then transferred onto Columbia blood plates (Barrett Biotechnology Co., LTD.) and allowed to incubate at 35°C in ambient air. Following colony growth, the mosses were chosen and determined using a Jiangsu Tianrui microTyper MS matter-assisted laser desorption ionization time-of-flight mass spectrometer. To monitor colony growth, the placenta and fetal swabs were inoculated on Columbia blood plates and incubated for 24 hours at 35°C ambient air temperature. The Gram staining microscope was used to monitor the growth of these bacteria, and mass spectrometry for identification.

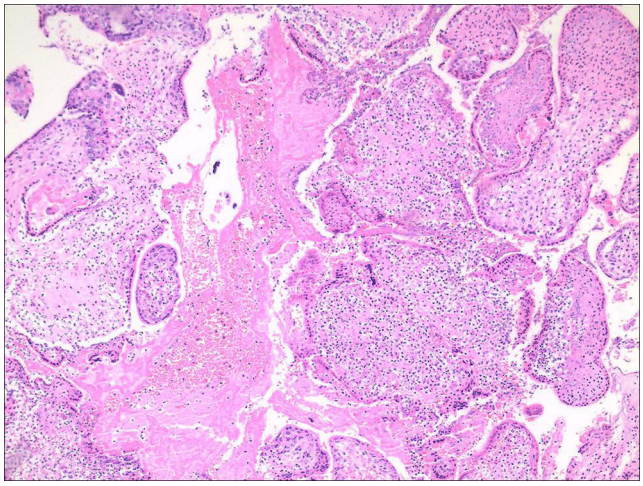

Figure 1 Acute diffuse villous inflammation accompanied by acute intervillositis (H&E× 100).

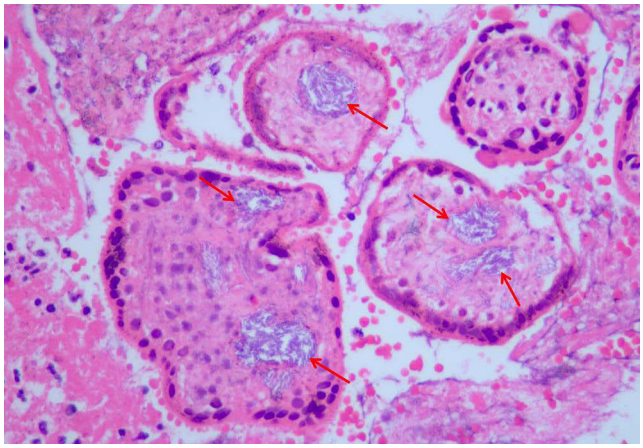

Figure 2 Placental villi showing villitis associated to the presence of bacterial organisms in fetal vessels (arrows) (H&E× 40).

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Discussion

Genetic amniocentesis during mid-trimester pregnancy is a frequently used procedure, though there may be some risks to the mother and fetus. The complication rate of fetal loss, bleeding and membrane rupture were 0.22%, 0.59% and 0.82%, respectively.[10] Despite the low complication rate of amniocentesis, subclinical intrauterine infections occur in up to 0.5% of patients after surgery.[11] In clinical intrauterine infection, acute chorioamnionitis or clinical intrauterine infections is more common. The three primary histological patterns of acute intrauterine infection include acute chorioamnionitis, acute intervillositis, and acute villitis. The condition causes maternal inflammatory response in the placental membranes and chorionic plates, as well as fetal inflammation, which manifests as funisitis, vasculitis of the chorionic plate vessels, and umbilical vessels.[3] Acute villitis is the rarest, and may be accompanied or not by chorioamnionitis or intervillositis. It is an indicator of fetal septicemia and has a higher risk of fetal morbidity and mortality than acute chorioamnionitis alone.[4]

We have reported a case of maternal septic shock and fetal death from *Bacillus cereus* infection following mid-trimester genetic amniocentesis. The placental pathological examination revealed evidence of acute chorioamnionitis along with a rare lesion: acute villitis. This lesion is associated with a high concentration of microorganisms in the fetal vessels of the chorionic villi and is strongly linked to fetal demise and detrimental maternal outcomes. An uncommon histological finding in the fetal capillaries of the chorionic villi is the presence of intravascular microorganisms, indicating that the bacteria were present in the fetal circulation during the fetus's life rather than postnatally or was a result of placental contamination.[12] In addition, maternal morbidity and death rates have been found to be significantly higher than those of any other intrauterine infection.[13] This suggests that fetal septicemia was severe enough to cause fetal death, as evidenced by the presence of intravascular microorganisms in the placental villi. Our case demonstrated what prior research has shown: acute villitis coupled with intravascular microorganisms in fetal vessels is invariably linked to fetal death, and it is more frequently discovered in the setting of uncontrollably high maternal sepsis.[4]

Maternal sepsis is defined as potentially fatal organ failure brought on by an infection that arises during pregnancy, childbirth, miscarriage, or the postpartum phase.[14] Ascending microbial invasion from the lower genital tract appears to be the most common pathway for intra-amniotic infection, and contiguous spread from chorioamnionitis is the most common cause of maternal sepsis. Very few cases of severe amniotic infection syndrome with septic shock and DIC after amniocentesis have been documented. The iatrogenic pathway, including amniocentesis, was thought to be the cause of the critical condition in our case, as the mother was in a state of septic shock, DIC, and fetal demise following the procedure. Through the process of amniocentesis, the organisms can enter the amnionic cavity. Once inside, they can cause either localized or systemic infection. Through the placental villous vessels, the organism can enter the fetal bloodstream as well as the bloodstream, causing septicemia.[15] Acute villitis, which was thought to be an unusual inflammatory fetal response, was present in conjunction with bacterial microorganisms in the fetal vasculature.[12] The fetal inflammatory response syndrome, which is the adult counterpart of the systemic inflammatory response syndrome, is defined by an increase in interleukin-6 concentrations in the fetal plasma.[16] In comparison to term gestations, the host response to microbial invasion of the amniotic cavity is stronger in preterm pregnancies.

Genital mycoplasmas, especially *Ureaplasma* species, *Gardnerella vaginalis*, and *Fusobacteria* species, are the most commonly occurring microorganisms in the amniotic cavity.[2] Relatively few cases of *Bacillus cereus*-related intrauterine infections have been reported, but when such infections do occur, they often exhibit clinically significant invasive characteristics. *Bacillus cereus* is widely distributed in the environment but is often overlooked as a contaminant by clinical laboratories and health care workers.[17] Since the seminal review published by Farrar in 1963, *Bacillus cereus* has gradually been recognized as a pathogen in clinical materials.[18] Its most well-known function as a human pathogen may be as a mediator of self-limited foodborne illness. Nonetheless, the growing recognition of *Bacillus cereus* as a pathogen that extends beyond the gastrointestinal tract and the increased risk of infection in neonates, intravenous drug users, immunocompromised individuals (such as those with AIDS and cancer), and those with artificial prostheses (such as orthopedic implants and cerebrospinal shunts) mean that the incidence of infections unrelated to food poisoning may increase in the coming years. Pneumonia, meningitis, sepsis, and bacteremia/sepsis are all severe clinical manifestations of extra-gastrointestinal *Bacillus cereus* infection, although these conditions are uncommon.[9] Given that children,

especially neonates, have immature immune systems and have multiple indwelling catheters, they have been identified as the group at highest risk for extra-gastrointestinal *Bacillus cereus* infection.[6] For example, Zhang et al[19] conducted the first in-depth analysis of late-onset neonatal sepsis caused by *Bacillus cereus*, revealing the high mortality associated with neonatal *Bacillus cereus* infection. It is noteworthy that in the field of obstetric infection, a series of new discoveries about *Bacillus cereus* have emerged recently. Xaplanteri et al[20] detected the presence of *Bacillus cereus* on the surfaces of medical instruments in the delivery room, such as operating table headrests and portable anesthesia machines. Additionally, one study[21] reported that the number of *Bacillus cereus* detected in pasteurized breast milk increased, indicating that heat treatment cannot completely inhibit *Bacillus cereus*, which may pose a potential threat to the health of newborns, especially for premature and low birth weight infants, who are at higher risk of infection.

Infection with *Bacillus anthracis* is known to result in fetal loss; however, no clear evidence of a comparable relationship has been found for Bacillus species other than anthracis. A case of severe, acute villitis and multiple gram-positive rods on the placenta's histologic evaluation was reported by Workowski et al.[18] The clinical course of the illness led to a caesarian section, where a viable but extremely preterm fetus was delivered. Lou et al[22] reported *Bacillus cereus* as a component of multiple-organism growth from cultures of postmortem fetal samples following intrauterine fetal demise as part of a larger review of 123 perinatal autopsies. Additionally, single-organism growth of an unidentified species of Bacillus from postmortem samples following intrapartum death was described in the review. A case of severe acute placental infection and fetal demise linked to invasive procedures involving *Bacillus cereus* was recently reported by Shea et al.[9] This instance highlights the significance of *Bacillus cereus* as a human pathogen, particularly highlighting its capacity to cause severe intraamniotic and placental infections that have detrimental effects on the developing fetus.

Our case highlights the importance of the peculiar pattern of placental intravascular organisms in acute intrauterine infection caused by *Bacillus cereus*, which is linked to a high rate of morbidity in mothers who develop sepsis. In the absence of other risk factors, previous research has demonstrated that the organism was most likely acquired nosocomially during mid-trimester genetic amniocentesis. Relative to the gestational age at birth, the prevalence of chorioamnionitis varies: it affects 3–5% of placentas delivered at term and 94% of placentas delivered between 21 and 24 weeks gestation.[2] Immune modulation associated with pregnancy may also participate in preterm pregnancies' vulnerability to infectious agents. Prompt antibiotic administration and early fetal delivery are necessary for optimal management of intrauterine infection to prevent serious adverse perinatal outcomes.[23] Because of the prompt administration of antibiotics and surgical intervention while under evaluation, our patient was able to survive without a hysterectomy. The examination of the placenta yielded important details regarding the cause and timing of the infection, as our case and other research have shown. In addition to improving our knowledge of the cause, course, and etiology of the inflammatory process, this analysis will aid with the obstetric care needed by these patients currently and in the future.

Ethics Approval

This case was approved for publication by the Human Research Ethics Committee of Women and Children's Hospital, Xiamen University (approval number: KY-2022-007-H01). Written informed consent from the patient was obtained for this study.

Consent for Publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

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Disclosure

The authors report no conflicts of interest in this work.

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