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CASE REPORT

Prenatal sonography of placental abscess and prolonged antibiotic treatment for *Serratia marcescens* bacteremia

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Key Clinical Message

Termination of pregnancy is indicated for *Serratia marcescens* bacteremia, a major cause of mortality. Our present case was highly challenging because the patient wished to continue with her pregnancy, and the ultrasonography showed features of a placental abscess. Although the outcomes were good after prolonged antibiotic treatment, this was an exceptional case.

Keywords

Bacteremia, chorioamnionitis, infection, prenatal diagnosis, prenatal ultrasonography, *Serratia marcescens*.

Introduction

Serratia marcescens, a Gram-negative facultative anaerobe, can cause nosocomial infection, usually in immunocompromised patients. *Serratia* bacteremia has a high mortality rate, with 6-month mortality rates of 37% [1]. *Serratia* bacteremia in pregnancy is a rare but potentially fatal disorder. Of six reported cases of *S. marcescens*-associated chorioamnionitis or placental abscess [2–7], four resulted in miscarriages and two in preterm deliveries before 29 weeks. Here, we report a case of placental abscess associated with *S. marcescens* bacteremia with subsequent delivery of an uninfected term baby after prolonged antibiotic therapy.

Case Presentation

A 35-year-old Chinese woman, gravida 4 para 1, with good past health, conceived naturally and was admitted at 15 weeks and 3 days for a 2-week history of recurrent fever with chills and rigor. She also had a runny nose, cough, sputum, headache, and myalgia and was vomiting undigested food.

On admission, her blood pressure was 96/54 mmHg, with a pulse of 121 beats/min and a temperature of 38.8°C. Physical examination was unremarkable; vaginal examination showed that there was no leaking of amniotic fluid. Marked ketonuria was found and corrected with fluid replacement. Blood was taken for full blood count, C-reactive protein (CRP), liver and renal function tests, clotting profile, and culture. Investigations showed a mildly increased white blood cell (WBC) count (11.4×10^9/L; normal range, 3.7–9.2 $\times 10^9$/L), a low hemoglobin level (9.9 g/dL), and a normal platelet count (173×10^9/L; normal range, 145–370 $\times 10^9$/L). Her liver and renal function tests and clotting profile were normal. Empirical antibiotics, intravenous 1.2-g vial of amoxicillin and clavulanate, were given every 8 h for suspected sepsis

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with an unknown source considering the high fever and leucocytosis.

On the next day, blood culture in anaerobic broth showed Gram-negative bacilli; therefore, 500 mg of intravenous metronidazole was added every 8 h. On day 2, her fever persisted with her temperature reaching 39.9°C and tachycardia of 139 beats/min. She started to have a small amount of vaginal bleeding followed by abdominal pain. Blood investigations showed a further reduction in the hemoglobin level to 7.8 g/dL, thrombocytopenia with platelet count of 98×10^9/L, a normal WBC count (4.2×10^9/L), an increased CRP of 197 mg/L (normal, <5), hypokalemia with potassium level of 2.6 mmol/L, and slightly increased prothrombin time and activated partial thromboplastin time. Antibiotics were changed to a loading of 1 g of intravenous meropenem and then 500 mg every eight hours. She was then transferred to the intensive care unit for maternal septicemia. Subsequently, *S. marcescens,* sensitive to ertapenem/cefepime, was identified in both the blood culture and a high vaginal swab. *Listeria* was excluded. Two units of packed cells were given. An ultrasound of the abdomen and pelvis showed no abnormalities. Culture of midstream urine, sputum, and nasopharyngeal swab and a chest X-ray with abdominal shield were all negative.

Obstetrical ultrasound examination showed a single viable fetus with a size appropriate for the gestational age, normal amniotic fluid, a normally located placenta without apparent retroplacental clots, and a cervical length of 2.8 cm. The option of amniocentesis to exclude chorioamnionitis and for bacterial culture was discussed but was declined by the patient, who was concerned about its associated miscarriage risk. The patient was counseled and informed of the fact that *Serratia* chorioamnionitis was associated with a high risk of miscarriage and recurrent infections even with an apparent good initial response to antibiotics [2–7]. The patient was decisive regarding continuation of her pregnancy. In view of the clinically suspected chorioamnionitis but without confirmation by amniocentesis, meropenem, given through a peripheral intravenous line, was increased from 500 mg to 1 g every 8 h, and its course was extended from 2 to 4 weeks. Her fever came down, and CRP, WBC, and platelet count all returned to normal. She was then transferred back to a general ward at 18 weeks' gestation. She was asymptomatic apart from persistent mild vaginal spotting. Repeated ultrasound examination showed a hypoechoic mass measuring $2.1 \times 1.6 \times 1.5$ cm with mild vascularization at the lower part of the placenta (Fig. 1A and B); that mass enlarged to 3.1×2.0 cm 1 week later. There were no gross fetal abnormalities. Options of amniocentesis or transabdominal aspiration of the placental mass to exclude chorioamnionitis and for culture were discussed again, but she declined these options. In view of the suspected placental abscess, the course of meropenem was increased from 4 to 6 weeks. The size of the mass remained static in two weekly ultrasound examinations. She tolerated meropenem well.

At gestation of 21 weeks and 4 days, meropenem was stopped after a 6-week course since the patient was asymptomatic, and all blood parameters were normal. However, on the same day, she developed vaginal bleeding and a fever reaching 38.2°C. Meropenem was thus resumed immediately. Her CRP was increased from 6 to 35 mg/L initially and then returned to normal 6 days later together with reduction in the fever and vaginal bleeding.

At 24 weeks' gestation, she experienced mild vaginal bleeding again. Repeated urine culture showed enterococcus that was sensitive to nitrofurantoin and vancomycin only. These two antibiotics were not preferred because of the possible adverse neonatal or fetal effects such as potential preterm delivery, making nitrofurantoin unsuitable; vancomycin was a pregnancy category C drug per the Food and Drug Administration. An intravenous dose of 300 mg of daptomycin, a category B drug, was thus given daily for 1 week.

She had recurrent episodes of mild vaginal bleeding at 26, 27 and 31 weeks' gestation. Meropenem was continued. Serial ultrasound examinations showed that the placental mass became less prominent than at 19 weeks and was reduced in size to 1.3×1.1 cm at 34 weeks' gestation. The fetal growth, umbilical artery, and middle cerebral artery Doppler studies were all normal.

Induction of labor was performed at 37 weeks' gestation, resulting in a vaginal delivery of a boy weighing 2.91 kg with normal Apgar scores. Gross examination of the placenta showed two whitish nodules over the fetal side beneath the fetal membrane, measuring $4.5 \times 2.3 \times 2$ cm (W1) and $3 \times 2 \times 1.2$ cm (W2) (Fig. 1C and D). On histopathologic examination, W1 represented the placental infarct. A swab from W1 grew scanty enterococcus species, sensitive to vancomycin, and a culture of the placental tissue biopsy from W1 showed scanty growth of enterococcus faecium. W2 represented the healed placental abscess. No micro-organisms were found on Gram, Grocott, and Ziehl–Neelsen stains. Viral inclusions or granulomas were not seen. No chorioamnionitis or funisitis was found. The placental swab for culture was negative.

The patient remained healthy. Repeated blood, urine, and vaginal swab cultures were all negative. Meropenem was finally stopped 2 weeks after the delivery.

The baby was given an injection of 0.29 million units of benzylpenicillin sodium every 12 h for 2 days and

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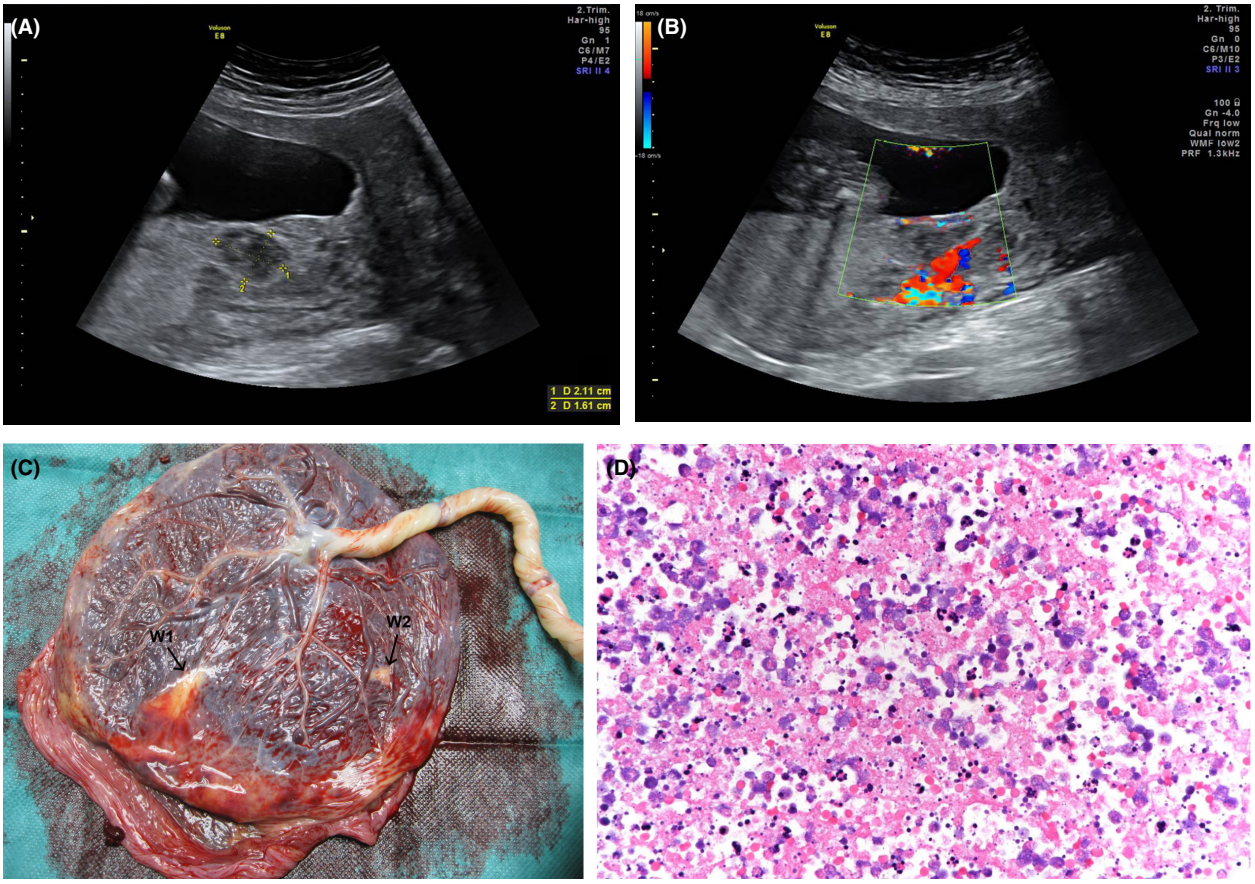

Figure 1. In *Serratia marcescens* bacteremia, ultrasound examination at 19 weeks' gestation showed a hypoechoic mass with an echogenic border (marked) (A) and vascularization (B) in the placenta. After delivery, (C) gross examination of the placenta showed two whitish nodules (W1 and W2) beneath the fetal membrane on the placental surface, and (D) histologic examination of W2 shows a healed placental abscess consisting of degenerated neutrophils and fibrin exudate (Hematoxylin and eosin staining, ×400).

58 mg of meropenem every 8 h prophylactically. Thirty milligrams of vancomycin was added every 8 h for a total of 5 days because the mother's placental abscess swab grew enterococcus. The sepsis workup, including WBC, CRP, blood culture, and lumbar puncture, was negative, and ultrasonography of the brain was normal. Meropenem was then stopped on day 5. The baby was healthy and was discharged with the mother.

Discussion

A placental abscess was suspected prenatally with abnormal ultrasound findings of an enlarging placental hypoechogenic shadow that decreased in size with continuation of meropenem and was confirmed subsequently on pathological examination of the placenta after delivery. Prenatal diagnosis of a placental abscess is rare and difficult and can be confirmed by aspiration of the lesion under ultrasound guidance [4]. Amniocentesis can show features of chorioamnionitis, but a negative result cannot completely exclude it especially at an early stage and may not predict the poor outcome of an affected fetus [4]. Additionally, these are invasive procedures with risks of miscarriage and transmission of the infection to the fetus.

Meropenem is compatible in pregnancy; all *Serratia* species are intrinsically sensitive to meropenem [8]. The latter was used in the present case and three of the six reported cases [4, 5, 7]. The optimal duration of antibiotics in treating *S. marcescens* bacteremia is unknown. Previous reports have suggested possible persistence of *S. marcescens* inside the chorioamnion and placental abscess after a short course(s) of antibiotics with a good initial response, resulting in recurrent bacteremia and miscarriage [3, 4]. Placental penetration of intravenous antibiotics might not be optimized [4]. Treatment failure and miscarriage have been reported [2, 6]. Carbapenem resistance, mainly by carbapenemase production, is uncommon in *Serratia* species [8]. In the present case, we increased the duration of meropenem from 2 to 4 weeks as a result of suspected chorioamnionitis, then to 6 weeks

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for suspected placental abscess, and subsequently to delivery because of recurrence of fever and per vaginal bleeding after a 6-week course. When the patient became asymptomatic and the placental mass smaller at 34 weeks' gestation, it was debatable whether meropenem could be stopped. We balanced the risks of inadequate antibiotic therapy against the potentially harmful effects of a prolonged course of antibiotics. Fortunately, the patient did not have any side effects apart from infrequent changing of peripheral intravenous lines for the administration of antibiotics. However, subsequent isolation of *Enterococcus* species urine cultures was most likely a result of meropenem selection because *Enterococcus faecium* is resistant to meropenem. In addition, the presence of *Enterococcus* species in the placental abscess and swab after vaginal delivery could be the result of colonization and contamination rather than true infection.

Similar to other cases [2, 6, 7], an ascending infection from the vagina most likely occurred in the present case because the vaginal swab culture showed *S. marcescens*. The latter is not part of the normal vaginal flora and can be acquired mostly within hospitals through the hands of personnel, contaminated irrigation solutions or disinfectants [9], chorionic villus sampling [2], repeated vaginal examinations after preterm prelabor rupture of membranes [7], or placement of a central venous line [4]. However, there was no such history in our present case.

We describe prenatal sonography of a placental abscess associated with *S. marcescens* bacteremia and term delivery of an uninfected newborn without funisitis after prolonged antibiotic therapy. When managing *S. marcescens* bacteremia in pregnancy, termination of pregnancy is an option to be considered because maternal sepsis is a major cause of mortality, and the fetal outcomes are largely unfavorable [2–7]. Our present case was highly challenging because the patient wished to continue with her pregnancy. Although the outcomes were good after prolonged antibiotic treatment, this is an exceptional case. Whether ultrasonography can detect placental abscess in association with other bacteremia [10] requires further studies.

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Ethics Approval

Ethics approval was not required.

Conflict of Interest

There is no conflict of interest for any parties.

Authorship

ASLM and KYL: involved in obstetric management. THCT, KWL, and TCW: involved in management of sepsis. ALMK and WC: involved in pathological examination of placenta. All authors contributed to manuscript preparation.

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