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Idiopathic massive fetomaternal hemorrhage in the third trimester of pregnancy causing neonatal death

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Summary

Fetomaternal hemorrhage (FMH), which can occur throughout pregnancy, is still a poorly understood clinical condition. It is very difficult to be timely diagnosed and often results in poor pregnancy outcomes. Here the authors reported two rare cases of silent massive FMH of unknown cause in the third trimester of pregnancy, which presented with non-reactive fetal heart rhythm or decreased fetal movement at the very beginning, and resulted in severe fetal anemia and neonatal deaths. A pregnant woman at late pregnancy with a complain of unspecific signs such as decreased fetal movement should arouse a high index of clinical suspicion of idiopathic FMH, and an urgent ultrasound or lab tests detecting FMH could be suggested. Considering emergent delivery versus expectantly management will depend upon acute or chronic FMH, gestational age, results of fetal testing, availability of experienced personnel, and procedural difficulty.

Key words: Fetomaternal hemorrhage; Fetal movement; Fetal anemia; Neonatal death.

Introduction

Fetomaternal hemorrhage (FMH) refers to entry of fetal erythrocyte into maternal circulation during pregnancy, which can cause fetal anemia and maternal hemolysis. It was first proposed by Wienes in 1948 and later was confirmed by Chown in 1954 [1]. Small amount of FMH which is less than 0.1 ml occurs in most pregnancies and it has no effect on fetus. Massive FMH greater than 150 ml can affect the pregnancy outcome by causing severe fetal anemia, unexpected stillbirth, and neonatal death. The perinatal mortality caused by massive FMH is up to 33~50% [1]. However, most cases of FMH are idiopathic or "silent" and may remain undiagnosed until delivery. The authors recently encountered two rare cases of silent massive FMH of unknown cause in the third trimester of pregnancy, which presented with non-reactive fetal heart rhythm or decreased fetal movement at the very beginning, and resulted in severe fetal anemia and neonatal deaths.

Case Report

Case 1, a 27-year-old woman, gravida 1, para 0, was admitted to hospital at 39+5 gestation weeks because of a small amount of vaginal bleeding with no associated abdominal pain or rupture of membrane over the preceding three days. During the pregnancy, there was no complications and exposure to any infectious agent or abdominal trauma or invasive obstetric procedures. Her blood type was A-type, Rh positive, with a recent negative antibodies screening. The cervix was found to be un effaced and undilated. Repeated fetal cardiotocograph (CTG) after admission showed non-reactive pattern with reduced variability of the baseline but the biophysical profile obtained by ultrasound was normal (score = 8/8). The fetal movement of maternal perception was normal too. Eighteen hours after admission, the fetal CTG showed non-reactive pattern with sinusoidal wave. The emergency cesarean section under general anesthesia was performed immediately for suspicious fetal distress. Severe meconium stained amniotic fluid was found during the operation. A very pale male infant weighing 3,200 grams was delivered without edema. Apgar scores were 6, 8, and 8 at one, three, and five minutes, respectively. The baby was transferred to the NICU immediately. The arterial pH, hemoglobin level, hematocrit and reticulocytes of the infant at birth were 6.91, 33 g/L, 11.7%, and 22.12%, respectively. The blood type of the baby was AB-type, Rh positive. Meanwhile, the authors found the maternal hemoglobin F (HbF) detected by high-performance liquid chromatography (HPLC) and α-fetoprotein (AFP) were 3.7% and >1000.0 ng/ml, respectively, which were much higher than normal. The estimated FMH volume was 185 ml [2]. The histopathology results of the placenta and umbilical cord were unremarkable. The baby required a number of blood transfusions, and suffered from severe acidosis, electrolyte disturbances, respiratory distress, hepatic failure and disseminated intravascular coagulation. However, the baby showed adverse reaction to the treatments including blood transfusion, fluid expansion, homeostasis correcting, and coagulation rectification, and died 48 hours after birth.

Case 2, a 29-year-old woman, gravida 1, para 0, was admitted to hospital at 38 +3 gestation weeks with decreased fetal movement. Regular prenatal care was normal and her blood type was B-type, Rh positive. She had a history of diminished fetal movement one day before admission without visiting doctor. She had neither abdominal pain, vaginal bleeding nor rupture of membrane. An infant was delivered by emergency cesarean section under general anesthesia two hours after admission because of non-reactive pattern with decreased variability of fetal CTG and low biophysical profile by ultrasound (score = 5/8). Severe meconium stained amniotic fluid was found during the operation. A very pale 2,600-gram female infant was delivered without edema.

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Apgar scores were 1, 3, and 5 at one, three, and five minutes, respectively. The baby was transferred to NICU immediately. The arterial pH, hemoglobin level, hematocrit, and reticulocytes of the infant at birth were 7.08, 29 g/L, 9.4%, and 10.11%, respectively. The blood type of the baby was O-type, Rh positive. Maternal HbF detected by HPLC and AFP were 4.3% and 1580.9 ng/ml, respectively, which were significantly higher than normal. The estimated FMH volume was 215 ml [2]. Histological examination of the placenta revealed non-specific chorangiosis, including little intervillous thromboses and calcification lesions. There were no signs of hemorrhage, vascular tumor or intraplacental hematomas. The umbilical cord was normal too. The neonate required intensive treatment, including a number of blood transfusions and ventilator support for severe acidosis, electrolyte disturbances, respiratory distress, hepatic failure, kidney failure, and disseminated intravascular coagulation secondary to massive FMH. The baby was in very serious condition after blood transfusion, fluid expansion, homeostasis correcting, and coagulation rectification. Intensive care was withdrawn at 72 hours after discussion with the parents, due to severe intraventricular hemorrhage.

Discussion

The two cases reported here were both rare massive FMH with unknown reason at late pregnancy which lead to severe fetal anemia and neonatal death. The incidence of massive FMH was estimated ranging from 0.2-0.9 per 1,000 births [3]. The real reason is unknown but it was speculated that a disruption of the trophoblast cell in the fetal-maternal interface may allow a large amount of fetal erythrocytes entering from the higher pressure fetal circulation into the intervillous space where they eventually enter into maternal circulation [2].

The risk factors causing FMH include blood type incompatibility, abdominal trauma, amniocentesis, external cephalic inversion, hypertensive disorders or placental and umbilical cord abnormalities, such as choriocarcinoma [4, 5]. However, the two rare cases reported here are idiopathic in origin, spontaneous, and uncomplicated near-term pregnancies.

Identifying the timing of the onset is very important in the management of FMH. Unfortunately, this issue seems to be unresolved by far. Observational reports suggest that a slow loss of up to 30% of blood volume for fetal can be tolerated and hydrops from anemia (fetal Hgb < 60 g/L) develop for several days (four to six days), while with acute blood loss the chance for fetal damage is significantly higher. Moreover, hyperacute hemorrhage occurring within minutes to an hour before delivery is fatal, and the Hgb and Hct for neonate at birth might be normal [6]. Thus, the lack of hydrops at birth in the two babies, despite a very low Hgb, may give some clues of the timing of the hemorrhage. The authors speculated that the hemorrhage in the two cases occurred within only one or two days before delivery.

Clinical presentations of FMH are frequently uncharacteristic and may be completely overlooked, thus diagnosis remains very difficult and relies mainly on a very high index of clinical suspicion. Decreased or absent fetal movements was the most common warning presentation. Next, a typical response is to perform a fetal CTG or biophysical profile. A non-reactive pattern of fetal CTG with reduced variability of the baseline has also been described as a presenting CTG abnormality in FHM patients [2]. Sinusoid pattern in fetal CTG and fetal hydrops, traditionally equated with severe fetal anemia, were classic presenting signs. In this study, only case 2 had a decrease of fetal movement, following non-reactive pattern of fetal CTG and low biophysical profile. In case 1, repeated non-reactive pattern of fetal CTG and sinusoid wave in the end prompted an emergent cesarean section, although the fetal movement and biophysical profile were normal after admission. Thus, selective or persistent monitoring of the fetal condition for suspected FMH is necessary. In both cases, there was no observable risk factor leading to massive FMH and it was not suspected by clinical doctor in the first instance and missed during the very moment of rescue. Unfortunately, negative neonatal outcomes were obtained in both cases, although the authors had performed emergency cesarean section as soon as possible and had transferred babies to NICU for the following intensive treatments.

Although rapid diagnosis of FMH may not be available as the clinical presentations are non-specific, the detection of HbF is helpful in the diagnosis and treatment of FMH. HPLC was developed in recent years for the separation and determination the concentration of HbF in maternal circulation, which is much more simple, rapid, and effective than the standard K-B test [7]. Maternal serum concentration of α-AFP is another simple and easy-detecting index of diagnosing FMH, but the levels vary significantly during pregnancy [8]. The concentrations of HbF and AFP in both cases of this report were significantly higher than normal, and massive FMH were confirmed by perinatal outcome. The value of Doppler sonography for the fetal middle cerebral artery (MCA) has been proven to predict fetal anemia recently. An increase of fetal middle cerebral artery peak systolic velocity (MCA- PSV) was considered as the sign of moderate or severe fetal anemia because of increased cardiac output and declined blood viscosity [4, 9]. However, these two cases were unsuspected for FMH at the very beginning, resulting in the MCA-PSV that was not timely examined. These cases raised the recommendation to all patients in the third trimester of pregnancy presenting with decreased fetal movements, and repeated abnormal fetal CTG or low biophysical score of unknown reason should have a HbF test for mother or MCA- PSV performed for fetus to identify silent FMH.

In summary, the authors report two rare cases of neonatal deaths of full term fetuses with uneventful antenatal periods, where idiopathic massive FMH was an unexpected finding. FMH is still a poorly understood clinical condition. A pregnant woman in late pregnancy with a complaint of unspecific signs such as decreased fetal movement should always be referred to hospital for fetal testing (fetal

CTG, biophysical profile or both). An abnormality on fetal testing with unknown reasons should arouse clinical suspicion of FMH, and an urgent ultrasound or lab tests detecting FMH should be suggested. Once diagnosis is suspected, appropriate management, for example, considering emergent delivery versus expectantly management will depend upon acute or chronic FMH, gestational age, status of fetal testing, availability of experienced personnel, and procedural difficulty [2]. Given the inherent unpredictability of FMH and its potential for perinatal death, delivery should be considered when the risks of continuing the pregnancy appear to outweigh the risks of prematurity.

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