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Case Report

Massive fetomaternal hemorrhage with a favorable neonatal outcome: a case report

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ABSTRACT

Fetomaternal hemorrhage (FMH) indicates the passage of fetal blood into the maternal circulation. In most pregnancies, small amounts of fetal erythrocytes can cross over to the maternal circulation without causing problems for the fetus. On rare occasions, massive FMH can occur and causes profound fetal and neonatal anemia, which associate with high perinatal morbidity and mortality. Herein, we present a case of massive fetomaternal hemorrhage and a favorable neonatal outcome. The infant was a late preterm male born via an emergency cesarean section due to fetal distress, he had severe anemia, and hypovolemic shock. He was successfully resuscitated and the anemia was adequately corrected through three PRBCs transfusions. Acute massive fetomaternal hemorrhage was diagnosed based on a positive Kleihauer-Betke test on the mother's blood. The infant had normal growth and normal developmental milestones in the subsequent visits up to the age of 18 months.

Keywords: Fetomaternal hemorrhage, Fetal anemia, Neonatal anemia, Kleihauer-Betke test, Flow cytometry, Sinusoidal pattern

INTRODUCTION

Minor fetomaternal hemorrhage occurs when a small quantity of fetal blood passed into the maternal circulation. It is a common and clinically insignificant finding that takes place in pregnancy and delivery. However, massive FMH is a rare condition, and can potentially lead to severe fetal and neonatal anemia, stillbirth, and hypoxic-ischemic encephalopathy.[1] Most cases of acute and chronic FMH are idiopathic in origin and involve uncomplicated near-term pregnancies. Nevertheless, FMH is more common after traumatic diagnostic amniocentesis, external cephalic version, abdominal trauma, preeclampsia, and cesarean delivery. The Kleihauer-Betke (KB) test is still the most common test used to detect the fetal erythrocytes in maternal circulation. Recently, flow cytometry analysis has been developed to detect HbF, and it correlates well with the Kleihauer-Betke test.[2] Massive FMH may be associated with an adverse neurological outcome; and the prognosis can be improved by early diagnosis, timely delivery, and adequate neonatal blood transfusion. But, in the case of a premature fetus, intrauterine transfusion can be performed.[3]

CASE REPORT

A 34-week preterm male baby with a low birth weight of 2.39 Kg was delivered via an emergency cesarean section to a 30-year-old mother, para 5+3. She was unbooked in our hospital but she had a follow-up in a private hospital. She was a heavy smoker and known to have bronchial asthma and hypertension. Her previous pregnancy had been complicated by preeclampsia for which labor was induced at 35 weeks of gestation. Her current pregnancy was complicated with gestational diabetes that was

managed by diet. There was no history of bleeding, abdominal trauma, or placental abruption. The mother presented to the emergency room with a history of decreased fetal movements for two days. She was admitted for fetal surveillance. During the assessment before delivery, the ultrasound study was normal. However, cardiotocography (CTG) showed a sinusoidal pattern with periods of deceleration (Figure 1). The baby was delivered flat with bradycardia and marked pallor, but he responded well to the resuscitation measures, and his Apgar score was 5 and 8 at 1 and 5 minutes, respectively. Cord blood gas analysis showed pH: 7.24, pCO2: 40 mmHg, HCO3: 17 mmol/L, and base excess (BE): -8 mmol/L. The hemoglobin (Hb) in cord blood was 2.4 g/dL. The baby developed respiratory distress and was shifted to NICU, where non-invasive positive pressure ventilation (NIPPV) was started. Physical examination revealed a very pale infant with tachypnea, tachycardia, and very low blood pressure. The rest of his examination was unremarkable. Umbilical vein catheter (UVC) was emergently inserted and the baby was given 10 mL/kg intravenous normal saline bolus and O negative packed RBCs (PRBCs) unite was urgently requested. The respiratory distress progressively increased and the baby had an episode of apnea with desaturation and bradycardia, so he was immediately intubated and connected to a mechanical ventilator. During the first hour of life, 15 mL/kg uncross-matched O negative PRBCs were urgently transfused. Blood samples had been drawn for blood gas analysis, complete blood count (CBC), blood culture, and other laboratory investigations. Empirical antibiotics (ampicillin and gentamicin) were commenced. The first blood gas analysis showed mixed metabolic and respiratory acidosis, but the metabolic element was the main. Sodium bicarbonate infusion was slowly administered. Dopamine (10 µg/kg/min) was required to maintain normal blood pressure. The baby underwent three PRBCs transfusions throughout the first 24 hours of life, which resulted in an increase in his Hb to 10.6 g/dL. Total parenteral nutrition was given on the second day of life as the baby was kept NPO for the first three days. The baby and his mother had AB Rh-positive blood groups and direct and indirect Coombs' tests were negative. The initial blood chemistry, renal function tests, liver function tests, and coagulation profile were normal. Blood culture was also negative. The metabolic screening was unremarkable. Chest X-ray, brain and abdominal ultrasound, and echocardiography showed normal findings. The CBC changes throughout the hospital course are shown in table 1.

The diagnosis of massive fetomaternal hemorrhage was suspected. Kleihauer-Betke test on the mother's blood was done, and it revealed the presence of fetal red blood cells with an estimation of fetal hemorrhage of about 630 mL. The baby's condition gradually improved, and he was successfully extubated on the third day of life, to nasal continuous positive airway pressure (CPAP). On the fourth day of life, the baby was on room air. Tube feeding was started initially, and he could achieve full oral feeding at the age of eight days. The baby was discharged home at the age of 11days, in good general condition, with normal physical and neurological examinations. His hemoglobin was 11.6 g/dL. The baby was given a regular outpatient follow-up with CBC tests. Initially, his hemoglobin gradually decreased and reached a nadir level of 7.6 g/dL at the age of 6 weeks, hence, iron therapy was commenced. On the subsequent visits, the hemoglobin increased gradually to reach normal levels. The follow-up of the child up to the age of 18 months showed normal growth and developmental milestones.

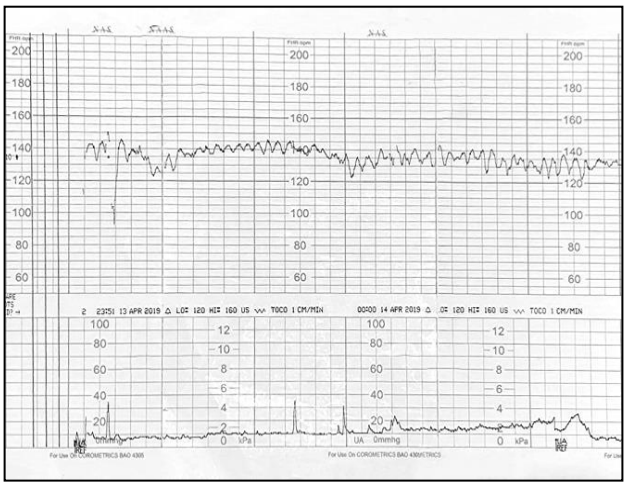

Figure 1: CTG showed a sinusoidal pattern with periods of deceleration.

Table 1: The successive CBC changes according to age.

Age	HB(g/dL)	HCT (%)	RETICS (%)	PLT ($\times 10^3/\mu L$)
1 hour (1st CBC)	3.8	13.2	15.38	101
3 hours (after1st transfusion)	4.8	16.2	12.5	104
24 hours	10.9	31	8.64	88
3 days	13.6	39.8	-	74
11days (At discharge)	11.6	34.9	2.82	358
6 weeks (Iron started)	7.6	23	-	300
7 weeks	8.1	23.5	4.48	386

DISCUSSION

The fetomaternal transfer of fetal blood cells exists, probably in all human pregnancies, but it seldom affects the normal course of pregnancy. However, massive fetomaternal hemorrhage can jeopardize the fetus and can cause an array of catastrophic consequences, including fetal death, hydrops fetalis, hypoxic-ischemic

encephalopathy, intrauterine growth restriction, and severe neonatal anemia.[4] Although there is no universally accepted definition of the volume of fetal erythrocyte transfer that constitutes FMH, blood volumes ranging between 10 ml and 150 ml have been proposed. Currently, the absolute volume of 80 ml or relative blood volume of 20 ml/kg is commonly used in the literature to determine the threshold for the amount of FMH sufficient to cause serious perinatal and neonatal morbidity and mortality.[5] Massive FMH is quite rare, and with using a common cutoff value of 30 mL for the diagnosis, the incidence of FMH has been estimated at 3 in 1000 pregnancies. The FMH is usually an underestimated and underdiagnosed obstetrical condition because of the lack of universal screening, variable clinical symptoms and signs, presentation as an immediate fetal compromise or stillbirth, and insufficient physicians' awareness.[6] The exact pathophysiology of fetomaternal hemorrhage remains obscure. FMH is hypothesized to occur via disruption of the placental trophoblast, through some unknown mechanisms, leading to the entry of fetal erythrocytes into the maternal circulation.[7] Several obstetrical events have been associated with FMH including external cephalic version, amniocentesis, abdominal trauma, placental abruption, placental tumors, and manual removal of the placenta. However, in up to 82% of cases of fetomaternal hemorrhage no causative agent can be identified.[5] A decrease or absence of fetal movement was the most common antenatal presentation of FMH. In the event of massive fetal blood loss, the mother may experience a transfusion reaction expressed as nausea, edema, fever, and chills.[7] Non-reassuring fetal heart rate tracing, fetal tachyarrhythmias, and sinusoidal patterns in CTG have been reported as indicators of fetal anemia but are not diagnostic of FMH as they are also associated with other conditions.[8] Massive FMH has a wide spectrum of clinical presentations depending on the volume of the hemorrhage and the rapidity with which it occurred. During chronic loss, the fetus has the opportunity to compensate in several ways, including increasing the production of red blood cells. However, in acute FMH, the rapid blood loss is followed by perinatal hypoxia and intrauterine fetal death, or severe neonatal anemia, and hypovolemic shock at birth.[9] The estimation of the FMH volume is very challenging. The rosette screen test can detect small quantities of fetal blood in the maternal circulation. However, Kleihauer–Betke acid elution assay remains the method of choice that can confirm the diagnosis and quantify the number of fetal cells.1 Recently, flow cytometry has been widely adopted as an FMH diagnostic tool because it is more sensitive and time-saving. In early pregnancy, increased alpha-fetoprotein (AFP) is a sensitive marker supporting the diagnosis of FMH. Currently, no laboratory test differentiates recently transfused fetal red blood cells from those having circulated longer.4 Middle cerebral artery peak systolic volume (MCA-PSV) measurement is an extremely valuable tool for detecting fetal anemia. This fast and reliable non-invasive tool in fetal assessment should be always incorporated in cases with suspicion of FMH.[10] Despite improvements in obstetrical and neonatal care, massive FMH is still very often a devastating obstetrical catastrophe leading to adverse pregnancy outcomes. In early pregnancy, intrauterine transfusion may be attempted to correct the anemia and it is effective and improves the prognosis. However, in cases of continuous bleeding, repeat transfusions or delivery may be indicated. It is of essential importance to notify the neonatologist in all cases of antenatally suspected massive FMH as the appropriate immediate resuscitation and blood transfusions are crucial to the outcome.[11] In cases of FMH with severe neonatal anemia, the treatment should follow an individual approach based on the patient's cardiovascular status, so that simple rapid transfusion is selected for cases of FMH with hypovolemia, and partial exchange transfusion with PRBCs is selected for cases of FMH without hypovolemia.[12]

CONCLUSION

Fetomaternal hemorrhage is a rare complication of pregnancy that may not be heralded by distinctive signs or symptoms. The only symptom that may be present is the mother's perception of a decrease in fetal movement. Doppler flow studies of the umbilical cord, a peak flow velocity on the middle cerebral artery, and a Kleihauer-Betke test on maternal blood are all helpful in diagnosis. The poor prognosis of massive FMH can be improved if this condition is early recognized and appropriately managed. We reported this case to address the clinical importance of this rare condition and to increase physicians' awareness aiming to improve the neonatal outcome.

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