Fetomaternal Hemorrhage: A Review after a Case Report

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Abstract

Fetomaternal hemorrhage consists in the transmission of fetal blood cells to the mother’s bloodstream. If it is quite common in small volumes — occurring in most pregnancies — large volumes of fetomaternal hemorrhage can have serious consequences. Some risk factors are identified, but they are not always present. Decreased perception of fetal movements is the most important clinical sign, together with a pathological NST. Prompt diagnostic and immediate obstetric cares are fundamental, as serious risks to the fetus might result from this condition.

We describe the case report of an eighteen-year-old primipara, 39 weeks pregnant, who referred reduced perception of fetal movements during the previous 6 hours. There was no history of abdominal trauma. Non Stress Test (NST) showed a sinusoidal pattern and an emergent C section was performed. A male infant with 3500 gr was born with an Apgar score of 5/7/7. Fetal hemoglobin at the first hour of life was 4.4g/dl. Kleihauer-Betke test revealed 6.7% of fetal erythrocytes in the maternal bloodstream.

Despite being rare, it is important to detect a massive fetomaternal hemorrhage. Fetal anemia could be suspected, but the diagnosis was only made after delivery. This case reveals the importance of keeping a high suspicion in obstetric practice, as fetomaternal hemorrhage is a rare but potentially catastrophic event for a fetus.

Keywords: Fetomaternal hemorrhage; Kleihauer-betke test; Fetal anemia

Introduction

Fetomaternal hemorrhage (FMH) consists in the transmission of fetal blood cells into the maternal circulation. Although the pathophysiology is not yet completely understood, it is likely to occur in small volumes in all pregnancies, with no apparent clinical significance in most cases [1]. The incidence of clinically significant fetomaternal hemorrhage varies widely depending on the cutoff used to define it [2]. Considering only the volume lost is probably insufficient as the rate of blood loss is also an important factor [3]. Many studies defined 30 mL as threshold for meaningful fetal blood volume and 80 mL or 150 mL as cutoff to define "large" or "massive" fetomaternal bleeds [2]. Massive fetomaternal hemorrhage is more likely to be fatal if blood loss occurs over minutes rather than hours, days, or weeks [4].

The blood pressure is higher in placental blood vessels than in the intervillous space. If the maternal-fetal barrier is disrupted, hemorrhage will occur from the fetus to the maternal circulation [3]. Incidence increases with gestational age, and so does the volume of fetal blood in the maternal circulation [1]. Some risk factors such as external cephalic version, abdominal trauma, manual removal of the placenta, placental abruption, monochorionic monoamniotic twins, preeclampsia, placental tumors, and amniocentesis have been associated with fetomaternal hemorrhage. However, no cause is identified in over 80% of cases [2].

Recognizing the bleed before it becomes significant requires a high index of suspicion as the triad of decreased fetal movement, sinusoidal heart rate, and hydrops fetalis corresponds to a group of symptoms of severe anemia associated with massive fetomaternal hemorrhage [3]. In some situations, such as unexplained stillbirth, persistent maternal perception of decreased fetal activity, hydrops, unexplained elevated middle cerebral artery Doppler, testing for fetomaternal hemorrhage should be considered [2]. Amongst the different diagnostic tests available, the Kleihauer-Betke is a quantitative test based on the principle that hemoglobin F (HbF) is relatively resistant to acid elution compared with the hemoglobin of adult erythrocytes [2].

When a massive fetal hemorrhage occurs it is crucial to promptly detect it. Immediate cesarean delivery is recommended if the infant is near-term gestation. In cases of preterm gestation, in utero transfusion can be considered to minimize the effects of fetal anemia [3]. If untreated, the effects of fetomaternal hemorrhage can be catastrophic, potentially resulting in cardiac failure, hydrops, hypovolemic shock, intrauterine demise, neonatal death, neurologic injury, cerebral palsy or persistent pulmonary hypertension [2].

Case Report

An eighteen-year-old primipara with an uneventful 39 weeks pregnancy was referred to our emergency department for skin purpitis. At admission she mentioned reduced perception of fetal movements during the previous 6 hours. There was no history of abdominal trauma and blood pressure was normal. Non Stress Test (NST) was non-reactive. It was decided to admit the patient for fetal surveillance.

Two hours later, during observation, the NST assumed a sinusoidal pattern (Figure 1 and 2— part I and II) and emergent C-section was performed. A male infant with 3500 gr was born with an Apgar score of 5/7/7. Umbilical cord gasimetry showed an arterial pH of 7.150 with base excess (BE) of 6.3mmol/l and hematocrit 18%. Fetal hemoglobin at the first hour of life was 4.4g/dl. Maternal work-up included hemogram, biochemistry panel, infection screening, blood group confirmation with indirect Coombs and Kleihauer-Betke test. Notably, Kleihauer-Betke test revealed 6.7% of fetal erythrocytes in the maternal bloodstream.

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Placental pathological examination demonstrated edematous villi and the presence of numerous erythrocytic precursors with moderate to severe erythroblastosis.

The newborn underwent red cell transfusion, after which hemoglobin levels were 13.5 g/dl. He was discharged from the hospital on the 14th day with short term follow-up at our pediatrics outpatient clinic.

**Discussion**

Fetomaternal hemorrhage was first established as a clinical entity during the 1940s and 1950s [5]. Massive FMH greater than 30ml occurs in only about 3 of 1000 pregnancies [6]. The volume of blood loss required to affect the fetus is variable and is related to the cause and to whether the loss is acute or chronic [7]. It has not been shown to directly correlate with perinatal morbidity or mortality [5].

Many studies demonstrate that the initial and most significant warning sign for FMH is the mother’s report of reduction in fetal movement [7]. As mentioned above, although various risk factors are identified, most cases occur without any identifiable cause [7]. For this reason it is vital to be aware of FMH even when no risk factors are found. Women should be advised to pay attention to fetal movements and to seek for medical care after any trauma.

As a medical practice, we should perform clinical evaluation and NST routinely after 32 weeks of pregnancy and after any suspicion of trauma. In particular, a sinusoidal fetal heart rate pattern has been associated with fetal anemia. However, it is not diagnostic of FMH as it can be present in other conditions [7] and it occurs in only approximately 10% of cases [5].

In this particular case, FMH was not immediately suspected at the time of admission, because no risk factors were identified, but the clinical findings were sufficient to admit the patient.

Evaluation of FMH includes its confirmation (with Kleihauer
Betke test or flow cytometry) as well as determination of fetal wellbeing. It is recommended to use the Middle cerebral artery peak systolic velocity (MCA-PSV) measurements to determine the severity of anemia, as some recent studies have shown it is more useful than Doppler evaluation of umbilical artery or biophysical profile, which can produce normal results even in cases of acute severe anemia [8].

The deterioration of the fetal heart tracing, with a sinusoidal pattern, determined the need to perform an emergent cesarean section. After delivery, the newborn was assisted by a neonatologist. The Apgar score was 5 at the 1st minute and 7 at 5th and 10th minute. The newborn was admitted in the intensive care unit and blood exams revealed fetal anemia, justifying the low Apgar score.

Several studies show that a pH below 7.0 is the threshold for clinically significant acidemia [1], which can be caused by a decrease in uteroplacental perfusion and hypoxia. Fetal anemia can be one of the causes. In this case, however, arterial pH was 7.150, which is within the normal range.

As previously mentioned, if there is suspicion of FMH, the presence of fetal cells in the maternal blood stream should be confirmed. Kleihauer-Betke is the most widely used test [9]. It is based on the principle that hemoglobin F (Hb F, present in fetal erythrocytes) is relatively resistant when exposed to an acid solution, appearing as cherry-red fetal cells while maternal cells appear as uncolored “ghost cells” [2,9]. The test result quantifies the percentage of fetal cells observed on a microscope. The volume of fetomaternal hemorrhage is estimated by multiplying the percentage of fetal blood cells by 5000 (the average maternal blood volume, in mL) [2]. In this case, there were 6.7% of fetal blood cells, corresponding to a transfusion of 335ml of fetal blood into the maternal bloodstream [2]. This test is labor intensive and may underestimate (advanced gestational age) or overestimate (maternal Hb F hereditary persistence, sickle-cell anemia, beta thalassemia) the extent of the hemorrhage [2].

Flow cytometry is an alternative quantitative test. It is based on the number of fetal cells (Hb F) bound to monoclonal antibodies, measured by fluorescence intensity [2]. It has a better precision than Kleihauer-Betke test but it may not be available in all hospitals. Therefore, despite its advantages, Kleihauer Betke test is still the most widely used because FMH is an emergent situation in which it is vital to obtain the results promptly.

It is important to refer that both these tests are still unable to address two crucial questions: when the hemorrhage happened, and whether it is an acute or a chronic situation. This has a major impact on treatment and prognosis.

Another important exam in obstetric practice is the analysis of the placenta. In cases of FMH placental pathology can show erythroblastosis in villi, which is a sign of significant fetal anemia [10]. In this case, besides the erythroblastosis, the placenta was also hydropic corroborating the diagnosis.

**Conclusion**

Fetomaternal hemorrhage is a rare condition but its actual incidence is probably underreported. Some risk factors are well identified, and in those situations the diagnosis is promptly made. However, in some cases no risk factors are found and the clinical findings are not enough to make the diagnosis before delivery. Therefore, it is very important to recognize signs of fetal distress and to keep all differential diagnoses in mind in order to have the best possible maternal and fetal outcomes.

**References**

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