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Case report 1

Massive feto-maternal haemorrhage: A case report

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Key words: haemorrhage, Kleihauer test, maternal and fetal circulations

Abstract

Feto-maternal haemorrhage (FMH) is the passage of fetal blood in to the maternal circulation during pregnancy or delivery. Aetiology is largely spontaneous with no cause but placental trauma is a known cause. Insignificant FMH may occur nearly in all pregnancies and there is no defined degree of fetal haemorrhage to define FMH. Most episodes involve very small quantities of blood but in some cases, the haemorrhage is acute and massive enough to compromise the fetus, resulting in fetal demise, stillbirth or severe neonatal anaemia causing circulatory shock or hydrops. Symptoms of a significant FMH can be subtle, non-specific and difficult to identify at onset. Diagnostic clues are anaemia at birth in an otherwise well baby with no or minimal jaundice. The most useful diagnostic tests are Kleihauer test on maternal blood to quantify fetal red cells in maternal circulation and blood film. This case is of a neonate born with severe pallor with a haemoglobin of 2.6 g/dL and no clinical or laboratory evidence of haemolysis. Kleihauer test revealed 10% fetal red cells in maternal blood accounting for 240 mL of FMH where approximately 90% of fetal blood has been transferred to maternal circulation. Baby was managed with blood transfusions and saved with minimal complications.

Introduction

Although maternal and fetal circulations are considered separate and distinct, a bidirectional flow occurs across the placenta between mother and fetus throughout pregnancy and is considered physiological. FMH is considered when there is a significant transfer of fetal red cells into maternal circulation[1]. It has an incidence between 1/300-1/1500 pregnancies and account for approximately 0.04% of stillbirths[1]. The incidence increases during pregnancy: 4%, 12%, 45% in 1st, 2nd, 3rd trimesters respectively and 60% during delivery[4]. The ability of fetal red cells to cross into maternal circulation was first hypothesized by Weiner in 1948 as '*Attention is called to a previously unrecognized entity, namely, severe anemia of the newborn caused by unapparent hemorrhage from the fetal surface of the placenta*'[2] and was later confirmed as a cause of neonatal anaemia by Chown in 1954[3]. We hope this case report will help to consider FMH in the differential diagnosis of fetal or immediate neonatal anaemia.

Case report

A 34-year-old woman delivered a term male baby at 37+ weeks of gestation by emergency caesarian section due to reduced fetal movements and neonatal distress following an uneventful antenatal period. There was no consanguinity. Antenatal ultrasound scans did not reveal any fetal abnormality. Birth weight was 2.9 kg. The baby was severely pale and floppy. Intra-venous access obtained immediately, blood for investigations were drawn and intra-venous fluids were started. Full blood count (FBC) revealed, severe anaemia with a haemoglobin (Hb) of 2.6 g/dL, red cell count (RBC) of $0.83x10^{12}$ /L, haematocrit (HCT) of 11.6%, mean corpuscular volume (MCV) of 119.8 fL, white blood cell count (WBC) of $40.3x10^{9}$ /L and platelets of $171x10^{9}$ /L. Baby was less active with cold peripheries hence, immediately admitted to the special care baby unit. Vital parameters and venous

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blood gas were normal. Blood transfusion was commenced immediately with the blood pack cross matched and preserved for mother prior to caesarian section. (Both mother and baby were O Rh-D Positive). Fifty-five milliliters (20 mL/kg) of packed red cells were transfused while awaiting investigation results. Detailed clinical examination did not reveal any significant abnormality. Blood film showed normochromic macrocytic red cells (physiological for age) with many polychromatic cells and 75% nucleated red cells. White blood cells and platelets were normal in number and morphology for age. (Figure 1) Reticulocyte count was 14%, total bilirubin was 0.93 mg/dL and direct Coombs test was negative with normal clotting and biochemistry. Maternal investigations were also normal. Kleihauer test in a maternal EDTA blood sample revealed 10% fetal red cells in maternal blood accounting for 240 mL of FMH (Figure 2).

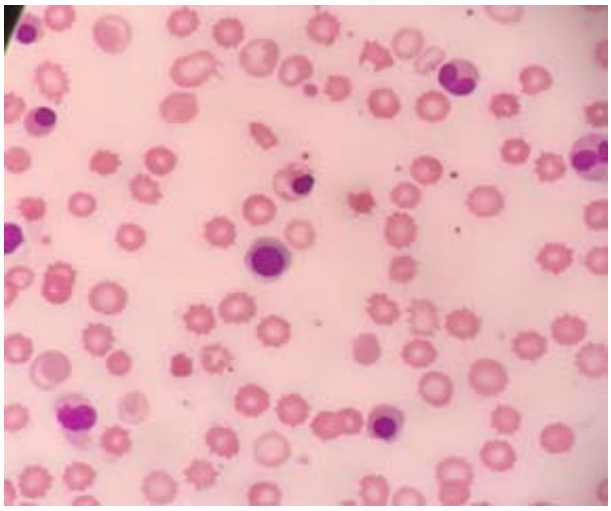

Figure 1. Blood film of the neonate at birth.

The baby's estimated blood volume was 246.5-261 mL. About 90% of fetal blood has been transferred to the maternal circulation. The baby was trans-fused with 3 more paediatric units (10 mL/kg) of packed red cells on next three consecutive days. Hb increased to 10.5 g/dL. Serum bilirubin raised to 7.9 mg/dL with indirect fraction of 7.3 g/dL. These levels were below photo therapy limits. The baby was pink, active and feeding well. Possibility of infections was excluded with normal cultures and inflammatory markers. He was discharged after one week with Hb of 13.5 g/dL. By day 14, bilirubin became normal and reticulocyte count was 7% By one month of age reticulocyte count was 1% while Hb and blood film appearances were normal for age and stable. The baby was growing normally with adequate feeding and weight gain therefore was discharged from the clinic.

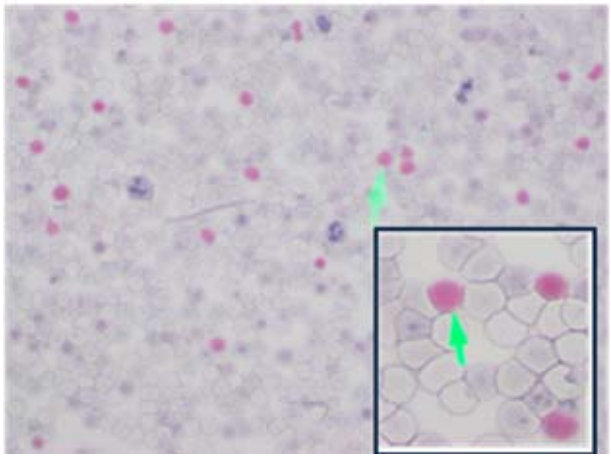

Figure 2. Kleihauer test x 40, insert x 100 (Arrow-Fetal red cells).

Discussion

There is no universally accepted degree of haemorrhage that defines FMH. Most women have very small amounts of fetal blood in their circulations following pregnancy and delivery. The volume is <0.5 mL in 93% of women, <1 mL in 96% and <2 mL in 98%. FMH >30 mL occurs in just 3 of 1000 women[5]. When >80 mL of blood is transferred FMH is considered massive[1]. Our patient had a massive FMH with 240 mL, three times of this cut off. As the degree of FMH has not shown a direct correlation with perinatal morbidity or mortality, defining significant FMH in terms of blood volume alone is not helpful[1]. There are more factors of concern other than the blood volume. Rate of blood loss, chronicity of bleeding and gestational age are other important factors in this context. Intravascular volume (calculated in mL/kg) varies throughout pregnancy; hence pre-term infants are at increased risk of adverse outcomes than term infants. They also have less ability to tolerate the stress associated with massive FMH[6].

Aetiology of FMH is multifactorial but most cases remain unidentified[1]. FMH physiologically occur as early as 4 weeks of gestation in combination of vascularization of chorionic villi and initiation of

contraction in the primitive heart. Fetal-placental blood vessels have higher blood pressure than the inter-villous space and in disruption of maternal-fetal barrier haemorrhage occurs from fetus to the maternal circulation[6]. Increased uterine activity during third trimester can result in microscopic capillary damage in placenta and allow trans-placental passage of fetal erythrocytes into maternal circulation[7]. Maternal abdominal trauma, obstetric procedures and surgeries (chorionic villus sampling, amniocentesis, intrauterine fetal operation, external cephalic version, cesarean section, manual removal of placenta, labour augmentation with oxytocin) and placental or implantation abnormalities (placental abruption, placenta-previa vasa-previa, chorio-angioma, threatened abortion) have been associated with increased risk of large FMH[7]. Association of FMH with intra-partum events like pre-eclampsia or placement of intra-uterine pressure catheter is also described. Massive FMH may recur in a subsequent pregnancy[4].

Majority of FMH occur with minimal signs and symptoms in apparently normal pregnancies. Reduced or absent fetal movement is the most common antenatal presentation as in our patient. Massive FMH can lead to adverse pregnancy outcomes such as intra-uterine growth restriction, hydrops fetalis, stillbirth, hypoxic-ischaemic encephalopathy, prematurity and severe neonatal anaemia. Nearly 50% of massive FMH are diagnosed in early neonatal period or when presented as fetal death. Fetal compromise can be detected by abnormal fetal heart rate and pattern, reduced beat to beat variability and very small CTG decelerations.

Clinical distinction between acute and chronic FMH is difficult, but significantly influence the management. In acute FMH, rapid fetal blood loss is associated with perinatal hypoxia or acidaemia that manifests as fetal or immediate neonatal anaemia, non-reassuring fetal heart rate patterns, haemodynamic instability and stillbirth or neonatal death[1]. In chronic FMH, fetus reacts by compensatory mechanisms. Increased haemopoiesis with increased production of erythroid precursors thus increased reticulocytes and nucleated red cells in peripheral blood which were evident in our patient, vascular redistribution of fetal blood flow with increased shunting of blood away from somatic circulation to brain, heart and adrenals (brain-sparing effect), abnormal middle cerebral artery (MCA) doppler velocity and fetal cardiovascular consequences such as increased heart rate, stroke volume, cardiac output and cardiac enlargement[1]. No serious clinical manifestations were present in our patient.

When there is blood group incompatibility between the fetus and the mother, in a massive FMH, mother may experience symptoms of acute transfusion reaction (nausea, vomiting, fever with chills, urticaria and angioedema)[6]. When haemorrhage occurs, maternal clotting activates as a reactive response limiting the effect of the haemorrhage, but in ABO-incompatibility activation of clotting is less likely and haemorrhage can continue[6]. In Rh-incompatibility, sensitization can occur and Rh immunoglobulin injection is indicated. Both mother and neonate were O Rh-D positive in our case.

Modified Kleihauer-Betke acid-elution test is the most widely used confirmatory test for quantifying FMH. It was first described by Kleihauer, Braun, and Betke in 1957, relies on the principle that fetal red cells containing mostly fetal haemoglobin (HbF), are resistant to acid-elution whereas adult haemoglobin with less HbF is acid-sensitive. Following incubation in an acidic solution, a sample of maternal venous blood is stained with erythrosine-B. Erythrocytes containing fetal haemoglobin appear red, while adult red cells look colourless (ghost). The fetal red cells are counted and reported as a percentage of adult cells. This test is inexpensive and requires no special equipment, but lacks standardization and precision. Increased HbF in maternal cells is seen in conditions like thalassaemia, sickle cell disease and hereditary persistence of fetal haemoglobin[9]. Flowcytometry is an alternative diagnostic method. It determines the number of fetal erythrocytes in maternal blood by measuring monoclonal antibodies binding to HbF in them. Advantages are improved interpreter objectivity, faster turnaround time and better accuracy. But its use is limited due to increased cost and decreased resources[9]. Most frequently used formula to determine the volume of fetal erythrocytes lost to the maternal circulation is to multiply the

percentage of fetal erythrocytes by estimated total maternal circulatory volume. Most formulas use average maternal blood volume as 5 L which varies significantly based on maternal weight, resulting in considerable variation in the determination of fetal volume lost. The degree of FMH can be underestimated in cases of feto-maternal ABO-incompatibility and iso-immunization, since fetal red cells that enter maternal circulation are rapidly cleared by maternal reticulo-endothelial system. Timing of FMH is difficult to ascertain as both methods do not address the question of when the fetal red cells entered maternal circulation[1].

Management of massive FMH depends on the gestational age of diagnosis, availability of cordocentesis for fetal blood sampling to diagnose fetal anaemia and perform fetal transfusion if needed and the capability of the neonatal intensive care unit[4]. If the fetus can compensate for blood loss, pregnancy may continue to delivery of an infant with varying degree of anaemia. In the setting of uncompensated anaemia, fetus may develop high-output heart failure and hydrops fetalis. In massive FMH, only hope for improved outcome is the prompt recognition and intervention. Unfortunately, symptoms are nonspecific and subtle. If fetal anaemia is recognized before delivery, risks and benefits of immediate delivery should be evaluated. If near-term, immediate delivery is indicated. Cesarean section is the delivery method of choice similar to our patient, because the compromised placenta may not support the stress of labour. If the fetus is preterm for delivery, in-utero transfusion can be considered. If haemorrhage continues, serial transfusions may be indicated. Determining the timing of subsequent transfusions is challenging since the rate of ongoing FMH is variable and unpredictable. Repeat Kleihauer test and MCA Doppler measurements too may be falsely low since transfused erythrocytes are also adult in origin[6].

When an infant is born with unexpected anaemia, alternative diagnoses such as haemolytic disease of the new born (ABO/Rh incompatibility), congenital infections resulting myelosuppression (TORCH) or bacterial sepsis too should be considered. Septic screening and empiric antibiotics are recommended. Congenital haemolytic anaemias (red cell membrane defects: hereditary spherocytosis and elliptocytosis; red cell enzyme defects: G6PD, pyruvate kinase deficiency), haemoglobinopathies (α-thalassemia) and congenital aplastic anaemia (Diamond-Blackfan syndrome) can also cause neonatal anaemia[6]. Most of these conditions can be diagnosed with readily available tests; direct Coombs test, reticulocyte count, septic screen, blood film morphology and HPLC. Neonatal anaemia has been reported as the presenting sign in 35% of FMH[6]. Hb <5 g/dL at birth has higher risk of poor outcomes (death, intravascular haemorrhage, periventricular leucomalacia, hypoxic ischaemic encephalopathy, broncho-pulmonary dysplasia). Fortunately, our patient did not develop any of these complications[10]. Signs of shock and circulatory failure can present with anaemia. Anaemia should be corrected slowly to avoid volume overload and exacerbation of heart failure. Exchange transfusion preferably with whole blood allows rapid correction of anaemia while avoiding complications associated with volume overload or cardiac compromise in severe cases. Citrate toxicity causing hypocalcaemia, clotting factor deficiency and thrombocytopenia occur as complications of massive transfusion, and calcium gluconate, protein and other blood products needs replacing. Our patient was successfully managed with top-up transfusions only. Rh-immunoglobulin should be administered to all Rh-negative women with suspected antenatal FMH in order to prevent sensitization.

As aetiology of FMH is unclear, it is difficult to ascertain the risk in future pregnancies for mother and difficult to recommend strategies to prevent recurrence. It is reasonable to counsel the patient on the importance of fetal movement counts and antepartum evaluation for evidence of fetal anaemia. This should include a reasonable schedule of non-stress tests and sonograms to assess for signs of anaemia and hydrops.

We report this case of massive FMH born with nonspecific symptoms and a very low haemoglobin for a surviving infant. Immediate detection of the condition, estimation of blood loss and blood transfusion helped saving the baby with minimal complications. This case is presented with the aim

of raising awareness of this condition among specialties involved to consider FMH in the differential diagnosis of fetal or neonatal anaemia with a comprehensive literature review.

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Conflict of interests

The authors declare no conflict of interests regarding the publication of this paper.

References

1. Case Report Acute and Chronic Fetal Anemia as a Result of Fetomaternal Hemorrhage. Singh P, Swanson T. Case Reports in Obstetrics and Gynecology Volume 2014, Article ID 296463, 4 pages http://dx.doi.org/10.1155/2014/296463
2. Wiener A S., Diagnosis and treatment of anemia of the newborn caused by occult placental hemorrhage. *Am. J. Obstet. Gynecol.* 1948; **56**(4): 717-22. [PubMed] [Google Scholar] https://doi.org/10.1016/0002-9378(48)90412-8
3. Chown B, Anaemia from bleeding of the fetus into the mother's circulation. *Lancet.* 1954; **266**(6824): 1213-15. [PubMed] [Google Scholar]
4. Troìaa L, Al-Kouatly HB, McCurdy R, Konchak P. S, Weiner S, Berghella V. Review: The Recurrence Risk of Feto maternal Hemorrhage. *Fetal Diagn Ther.* 2019; **(45)**: 1-12. DOI: 10.1159/000491788
5. Sebring ES, Polesky HF. Fetomaternal hemorrhage: incidence, risk factors, time of occurrence, and clinical effects. *Transfusion.* 1990; **30**(4): 344-57. DOI: 10.1046/j.1537-2995.1990. 30490273444.x
6. Solomonia N, Playforth K, Reynolds E.W. Fetal-Maternal Hemorrhage: A Case and Literature Review. *AJP Rep.* 2012; **2**(1): 7-14. DOI: 10.1055/s-0031-1296028
7. Heise R.H, Van Winter J. T, Ogburn P. L Jr. Case Report Identification of Acute Transplacental Hemorrhage in a Low-Risk Patient as a Result of Daily Counting of Fetal Movements. *Mayo Clin Proc.* 1993; **(68)**: 892-894.
8. Ahmed M, Abdullatif M. Fetomaternal Transfusion as a Cause of Severe Fetal Anemia Causing Early Neonatal Death: A Case Report. *Oman Med J.* 2011; **26**(6): 444-6. DOI: 10.50010/omj.2011.113
9. A. Kim, Robert S, Yeowon M. Detection of fetomaternal hemorrhage. *Am. J. Hematol.* 2012; **(87)**: 417-23. DOI: 10.1002/ajh.22255
10. Miyahara J, hi Sugiura H, Ohki S; Survival of an infant with massive fetomaternal hemorrhage with a neonatal hemoglobin concentration of 1.2 g/dL without evident neurodevelopmental sequelae. *SAGE Open Medical Case reports.* 2020; **(8)**: 1-3. https://doi.org/10.1177/2050313X20941984