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Case Report

Neonatology Section

Partial Exchange Transfusion in the Management of a Preterm Neonate with Severe Anaemia from Acute Foetomaternal Haemorrhage: A Case Report

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ABSTRACT

Foetomaternal Haemorrhage (FMH) refers to the passage of foetal blood into the maternal circulation. FMH is rarely diagnosed antenatally as clinical findings are subtle and non specific. Massive FMH is suspected when foetal movements are decreased, and Cardiotocographic (CTG) findings are abnormal with decreased heart rate variability, saw-tooth or a sinusoidal pattern. Massive FMH can lead to foetal demise, stillbirth, hydrops, or the birth of a severely anaemic infant with hypovolaemic shock. A 35-week pregnant woman presented with decreased foetal movements, and an emergency caesarean section was performed due to late deceleration on the cardiotocograph. The baby was very pale at birth and in shock. The Kleihauer-Betke (KB) test performed on the mother's blood shortly after delivery showed 2.7% foetal red cells, suggesting 135 cc of FMH. The clinical features and outcome of FMH depend on the gestational age, volume, and rapidity of FMH, as well as, whether it is acute or chronic. Packed cell transfusion is recommended, but in babies with severe anaemia and cardiac failure, partial exchange transfusion is performed. The baby was managed with a fluid bolus, inotropic support, respiratory support, and partial exchange transfusion, resulting in a successful outcome. A high index of suspicion enables the obstetrician to undertake diagnostic tests, cordocentesis, plan for intrauterine transfusion or delivery, and alert the neonatal team for a better outcome.

Keywords: Bleeding, Foetal movement, Hypovolaemic shock, Maternal circulation

CASE REPORT

A late preterm baby, born at 35 weeks of gestation, was retrieved from a private hospital at 30 minutes of age due to respiratory distress and pallor. This baby was born to a 26-year-old primigravida mother by emergency caesarean section done because of foetal distress. The antenatal period was uneventful until 12 hours prior to delivery when the mother noticed decreased foetal movements and the cardiotocograph showed late deceleration. There was no significant family or antenatal history.

There was no evidence of abruption, the placenta was pale, and the amniotic fluid was clear. The baby required positive pressure ventilation for one minute, and the Appearance, Pulse, Grimace, Activity and Respiration (APGAR) scores were 1, 3, and 8 at 1, 5, and 10 minutes, respectively. The baby was pale with a birth weight of 2100 grams. The baby developed respiratory distress soon after birth and was shifted to the Neonatal Intensive Care Unit. On examination, the vital signs were as follows: temperature 97.2°F, heart rate 162 beats per minute, respiratory rate 64 cycles per minute, blood pressure {Non invasive Blood Pressure (NIBP)} 42/26 mmHg (mean of 30 mmHg), and Saturation of Peripheral Oxygen (SPO_2) of 92% in Fraction of Inspired Oxygen (FiO_2) of 0.60. The baby exhibited clinical features of shock, including cold extremities, low volume pulses, and a delayed capillary refill time of 5-6 seconds.

Arterial Blood Gas (ABG) showed severe mixed acidosis, and a Complete Blood Picture (CBP) showed severe anaemia [Table/Fig-1]. As the respiratory distress worsened, the baby was commenced on Synchronised Intermittent Mandatory Ventilation (SIMV) mode of mechanical ventilation. Due to severe anaemia, shock, and haemodynamic instability, a partial exchange transfusion was performed with 75 mL of O group Rhesus negative packed red blood cells at four hours of life. The post-transfusion Haemoglobin (Hb) level was 13.9 gm/dL with a Haematocrit (Hct) of 42%. Shock was managed with a saline bolus and inotrope (adrenaline infusion). The baby had mild jaundice, and the maximum bilirubin level was 11.2 mg/dL on day 5 of life, which required no specific management.

Arterial Blood Gas (ABG)		Complete Blood Picture (CBP)	
pH	7.01	Hb	5.6 gm/dL
PCO_2	58 mmHg	Hct	15.2%
PO_2	42 mmHg	WBC	32400 cells/mm^3
HCO_3	11.2 mmol/L	Platelet count	1.29 lakh cells/mm^3
Base excess	-19.2	Nucleated RBC	64/100 WBC
Lactate	10.2 mmol/L	Reticulocyte count	7.2%

[Table/Fig-1]: Investigations done at admission. (ABG and CBP).
PCO_2: Partial pressure of carbon dioxide; PO_2: Partial pressure of oxygen; HCO_3: Bicarbonate; WBC: White blood cells; RBC: Red blood cells

The thyroid profile was normal, and there was no blood group incompatibility in the baby. Serology for toxoplasma, rubella, cytomegalovirus, herpes and parvovirus B19 infections was negative, and the direct Coombs test was negative. The blood groups of the baby and mother were O Rhesus positive. The KB test performed on the mother's blood sample shortly after delivery showed 2.7% foetal red cells, which corresponded to 135 cc of FMH.

The baby was extubated at 52 hours of life; however, the baby had feeding intolerance. The baby was on antibiotics for 72 hours, and subsequent sepsis screens were negative. The blood culture was found to be sterile. The baby reached full enteral feeds on day 9 of life, and the subsequent course was uneventful. The baby was discharged on day 10 of life, and growth and development were normal at six months of age on follow-up.

DISCUSSION

Spontaneous FMH is defined as the transfer of foetal blood into maternal circulation without trauma or placental abruption [1].

The ability of foetal red cells to enter maternal circulation was first reported by Wiener in 1948 and later confirmed by Chown B in 1954 [2,3]. The majority of FMH cases are of low volume (<0.1 mL) and occur in 39-98% of pregnancies without haemodynamic significance, but they can cause alloimmunisation. FMH of >20 mL occurs in 4.6 per 1000 live births, and >80 mL occurs in 0.7 per 1000 live births. Massive FMH, defined as >150 mL of foetal haemorrhage, occurs in 1 per 5000 live births. FMH is associated with nearly 14% of foetal deaths and 12.5% of stillbirths [4].

When FMH is suspected, maternal blood is tested for foetal red cells, and the most common test performed is the acid elution or KB test. In this test, maternal blood is fixed, washed with acid, and stained. The maternal cells appear as ghost cells, which are manually counted, and FMH is calculated based on the percentage of foetal cells. The KB test is influenced by temperature, pH, staining, intrauterine transfusion, maternal Foetal Haemoglobin (HbF) level, and can overestimate blood volume, with FMH volumes of 400-700 mL reported in the literature [1,5].

Other tests include the rosette test, flow cytometry, High-Performance Liquid Chromatography (HPLC), and serum alpha-foetoprotein [6]. The rosette test is a qualitative test, and if positive, it warrants a quantitative test. Flow cytometry is more accurate than the KB test but is not widely available [7]. Following FMH, α-fetoprotein levels increase in maternal serum, which helps estimate the volume of FMH [8].

The baby in this case was severely anaemic and required resuscitation, fluid bolus, inotrope, and respiratory support. Hence, a partial exchange transfusion was performed instead of a blood transfusion. Naulaers G et al., performed partial exchange transfusions in two neonates with severe anaemia due to massive FMH [9]. Naulaers G et al., also reported 100 mL of FMH in a 34-week preterm neonate with an Hb of 5.6 gm/dL, similar to the index case, but the neonate was treated with Packed Red Blood Cell (PRBC) transfusion as they were stable [9]. Miyahara J et al., performed a partial exchange transfusion with successful outcomes in a preterm neonate with severe anaemia (Hb-1.2 gm/dL) due to FMH [10]. The volume of partial exchange transfusion is calculated according to the formula: Volume of packed cells to be transfused=blood volume×(Desired Hct-Observed Hct)/(Hct of packed cells-Observed Hct) [11].

Other rare causes of anaemia, such as intrauterine infections and maternal parvovirus infection, were ruled out by viral studies. FMH is calculated using the formula: Stained cells/unstained cells×maternal blood volume=FMH in mL. One foetal cell per 1000 maternal cells (0.1% foetal cells) corresponds to 5 mL of FMH [12]. The index case had severe anaemia (Hb-5.6 gm/dL), and the KB test showed 2.7% foetal cells, which corresponds to 135 mL of FMH, representing a blood loss of 51.9 mL/kg.

The initial symptoms of acute FMH are often subtle and non specific. Occasionally, the mother presents with fever, chills, and nausea, which suggests a transfusion reaction. The triad of decreased foetal movement, sinusoidal heart rate and hydrops foetalis suggests massive FMH [13]. Disruption of the maternal-foetal barrier leads to FMH, as the blood pressure in foetal blood vessels is higher than in the intervillous space. In the setting of ABO incompatibility, the maternal clotting system is activated, and placental clots limit FMH. FMH can occur following maternal abdominal trauma, chorioangioma, abruption, monozygotic twins, and as a result of obstetric procedures such as external cephalic version, amniocentesis, and manual removal of the placenta. Severe FMH can lead to hydrops, disseminated intravascular coagulation, hypoxic-ischaemic encephalopathy, cerebral infarction, intraventricular haemorrhage, and periventricular leukomalacia. The differential diagnosis of neonatal anaemia includes haemolytic anaemia, congenital viral infections, erythrocyte membrane defects, red cell enzyme defects, haemoglobinopathies, congenital hypoplastic anaemia and leukaemia [14].

The management of massive FMH depends on gestational age, the availability of facilities for cordocentesis, foetal transfusion, and neonatal care. FMH at ≥34 weeks gestation with foetal distress warrants immediate delivery. At ≤32 weeks of gestation, Intrauterine transfusion (IUT) can be considered, if facilities are available. If the haemorrhage continues, serial transfusions may be indicated. Exchange transfusion allows for rapid correction of anaemia without volume overload or cardiac compromise [9-11].

Literature search showed that neonates with Hb <4.5 g/dL are associated with a poor outcome, and babies with Hb >4.8 g/dL had a normal neurodevelopmental outcome. Christensen RD et al., reported a normal outcome in neonates with Hb >4 g/dL and adverse outcomes if Hb was <4 g/dL [15]. The importance of foetal movement counts should be emphasised during counseling in the third trimester. Non stress tests, sonograms and doppler studies help assess foetal anaemia and guide obstetric management. The findings in the present study are compared with previous studies in [Table/Fig-2] [5,9,10,14].

Variables	Case-1 Solomonia N et al., [5]	Case-2 Miyahara J et al., [10]	Case-3 Gică N et al., [14]	Case-4 Naulaers G et al., [9]	Case-5 Naulaers G et al., [9]	Present case
Place and year of the study	Kentucky, 2012	Japan, 2020	Romania, 2021	Belgium, 1999	Belgium, 1999	India, 2023
Gestation	28 weeks	27 weeks	37 weeks	39 weeks	34 weeks	35 weeks
Birth weight	1335 g	998 g	3050 g	2450 g	2630 g	2100 g
KB test (% of foetal cells)	3.8%	2.4%	Not reported	4.5%	Not reported	2.7%
Volume of FMH	190 cc	120 cc	490 cc*	225 cc	100 cc	135 cc
Hb at birth	1.4 g/dL	1.2 g/dL	3.6 g/dL	3.7 g/dL	5.6 g/dL	5.6 g/dL
Haematocrit at birth	5%	4.5%	12%	11.3%	18%	15.2%
PRBC transfusion	15 mL/kg prior to ET	15 mL/kg prior to ET	90 mL transfused	Nil	50 mL PRBC	Nil
Partial exchange transfusion	Done with PRBC	Done with PRBC	Not done	Done with whole blood	Not done	Done with PRBC
Post-transfusion haematocrit	35%	27%	32%	37%	40%	42%
Additional transfusions	Platelet and PRBC transfusions	Nil	Nil	Nil	Nil	Nil
Treatment	Ventilation, Nitric oxide	Ventilation	Ventilation	Ventilation	Supportive care	Ventilation
Morbidity	Grade IV IVH, PHH	Nil	Nil	Nil	Nil	Nil
Outcome	NDI	Normal at 18 months	Normal at 6 months	Normal	Normal	Normal at 6 months

[Table/Fig-2]: Comparison of cases of FMH: Clinical features, laboratory investigations, volume of FMH and management [5,9,10,14].
ET: Exchange transfusion; IVH: Intraventricular haemorrhage; PHH: Post haemorrhagic hydrocephalus; NDI: Neurodevelopmental impairment
*490 cc was calculated based on anti-HbF flow cytometry value of 98.6%

CONCLUSION(S)

The FMH should be considered when a pregnant mother presents with decreased foetal movements, foetal distress, and a pale baby at birth. Although the symptoms of FMH can be subtle and non specific, reduced foetal movements, abnormal CTG, Coombs-negative anaemia, and the KB test can help diagnose FMH. Despite the limitations of the KB test, it helps quantify FMH. Partial exchange transfusion with PRBC is preferred over transfusion in unstable babies. Maintaining a high index of suspicion for FMH, monitoring CTG, considering emergency delivery, and providing resuscitation, stabilisation, and partial exchange transfusion in unstable babies improve outcomes without adverse effects.

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