Life-threatening neonatal anaemia following severe acute feto-maternal haemorrhage

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Introduction

A healthy placenta is capable of keeping the cellular components of fetal and maternal circulations separate[1]. Insignificant amounts of fetal blood enter the maternal circulation during a normal pregnancy and delivery[1-5]. Feto-maternal haemorrhage (FMH) occurs when a significant amount of fetal blood enters the maternal circulation, before or during delivery[1,2]. It is a poorly understood condition, resulting in anaemia, death or life-long disability in neonates[1-3]. Moderate to severe FMH occurs in 1-3 per 1000 live births[1,4]. FMH can cause hydrops fetalis, still birth or neonatal death due to resulting anaemia. It accounts for 14% of fetal deaths[1-3,5-7].

Presentation is often without an evident precipitating factor[2]. Commonest prenatal presentation is reduced fetal activity, thus warranting a high index of suspicion and appropriate management[2,5-7]. Detecting fetal blood in maternal circulation depends on the quantity of blood transferred, time during which transfer occurs and presence or absence of maternal antibodies to fetal red blood cells[1]. Management is challenging when detected prenatally; cordocentesis with intrauterine transfusion can be tried; however, delivery may be necessary to correct ongoing bleeding[2]. We report a neonate with severe anaemia following acute FMH.

Case report

A 29 year old mother, with O positive blood group, in her 2nd pregnancy was admitted at 33 weeks of gestation with reduced fetal movements of 8 hours duration. This was a planned pregnancy, and antenatal period, including all antenatal scans (latest at 29 gestational weeks), were uncomplicated up to time of presentation. Her first pregnancy was uncomplicated. Parents were healthy and non-consanguineous. There was no family history of haemolytic diseases or bleeding disorders. There was no history of trauma during pregnancy. Mother was not pale and examination was normal. Fetal heart sounds were normal. Ultrasound scan (USS) of abdomen did not show placental abruption. There was good antero-grade umbilical blood flow. Cardiotocogram showed pathological decelerations necessitating emergency caesarean section, following one dose of dexamethasone 12mg.

A severely depressed baby girl with Apgar scores of 1, 3 and 5 at one, five and ten minutes respectively, was delivered with a birth weight of 1900g, length of 41cm and occipito-frontal circumference of 30cm. All three basic anthropometric measurements were in between median to +1SD, suggesting that the baby was adequately grown for the age. She was extremely pale and was in circulatory collapse needing extensive resuscitation including intubation and ventilation. Resuscitation included administration of 10ml/kg normal saline boluses twice, urgent transfusion of 20ml/kg of uncross-matched O negative blood (subsequently, her blood group was confirmed as 0 positive), full correction of acidosis as the cord blood gas showed significant metabolic acidosis with a partial respiratory compensation (pH 6.93, pCO_2 15mmHg, pO_2 43mmHg, bicarbonate 11mmol/L, base excess 17mmol/L and lactate level 10mg/dL) and two 10ml/kg of fresh frozen plasma transfusions along with dopamine 10µg/kg as inotropic support. Her initial blood glucose value was 24mg/dL needing one 10% dextrose bolus followed by intravenous infusion of 10% dextrose 80ml//kg/day. Subsequent blood sugar values along with arterial blood gas values were normal throughout the neonatal intensive care unit (NICU) stay. Investigations revealed an initial haemoglobin (Hb) level of 1.8g/dL and a haematocrit of 6.3%. After packed cell transfusion at resuscitation and two further 10ml/kg blood transfusions, a Hb level of 16.1g/dL was achieved. Blood picture revealed normochromic normocytic anaemia with no evidence of haemolysis. Table 1 gives a summary of the basic investigations

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Table 1: ***Summary of basic investigations***

Investigation	Day 01	Day 10
Haemoglobin (g/dL)	1.8	16.1
White cell count ($\times 10^3/\mu L$)	4.3	10.2
Neutrophil count (%)	72	47
Lymphocyte count (%)	28	53
Platelet count ($\times 10^3/\mu L$)	98	202
Reticulocyte count (%)	0.02	2.2
C-reactive protein (mg/L)	<6	10
Aspartate transaminase (U/L)	73	25
Alanine transaminase (U/L)	100	58
Total serum bilirubin (µmol/L)	102.2	65
Serum sodium (mmol/L)	133	143
Serum potassium (mmol/L)	4.9	4.0
Blood urea (mmol/L)	6.1	2.5
Serum creatinine (µmol/L)	88.2	34
Prothrombin time (seconds)	15.5	12
International normalization ratio	1.6	1.2
Activated partial thromboplastin time (seconds)	42	37

Rubella, toxoplasma and cytomegalovirus IgM levels were not detected .and Venereal Disease Research Laboratory (VDRL) testing and parvovirus B19 Polymerase Chain Reaction (PCR) were negative. USS of brain and abdomen did not show evidence of internal haemorrhage. Modified Kleihauer-Betke (KB) test was strongly positive with an estimated fetal RBC percentage of 1.2%, corresponding to an approximate FMH over 60ml.

Kleihauer calculations:

1. % fetal red cells = fetal cells counted in total slide ×100/total maternal cells
2. Volume of FMH = % fetal red cells×5000ml (maternal blood volume) /100

The baby was weaned off the ventilator and discharged home in good health on day 10 of life. Currently, the baby's age is 1 year and her weight gain and development are satisfactory.

Discussion

The diagnosis of FMH is highly dependent on physician awareness[3,8,9]. Decreased or absent fetal movements reported by mothers is the commonest presenting symptom and is present in 54% of cases[3]. However, whether abnormal fetal biophysical profile should be taken as a factor to screen for possible FMH is doubtful, as 'non-reassuring' classic fetal heart rate pattern associated with severe fetal anaemia (resembling a sine wave) is seen only in 3% of cases[3].

Correct diagnosis is imperative for risk stratification of affected neonate, family planning and increased obstetric surveillance in future pregnancies and to establish epidemiologic predictors for the condition[1,3,9]. Diagnosis needs specific blood testing of mother and the KB test should be performed soon after birth to confirm the diagnosis[1-5]. Anti-HbF flow cytometry for fetal cells in the maternal circulation, which is not readily available in many hospitals, including the developed world, owing to the equipment and staffing costs, offers a simple, reliable and more precise alternative to the KB test[1,3,10]. If available, flow cytometry on women presenting with absent/reduced fetal movements, would help to alert the transfusion services[10]. Diagnosis within hours of birth is of value to establish the cause of anaemia and to estimate the volume of blood loss[3].

Severity of FMH has classically been graded by the volume of fetal blood loss rather than the clinical status of the newborn[1]. Though the exact volume of blood loss required to grade FMH as 'severe' is debatable, the volume of haemorrhage is directly proportionate to rates of adverse perinatal outcome[1,3,5,7,8]. However, outcome is better predicted by initial haemoglobin than volume of FMH[8]; 20-30% of affected neonates have one or more of these outcomes viz. hydrops fetalis, still birth or neonatal death, due to resulting anaemia, with greater odds of a poor outcome if born preterm or with a Hb<3g/dl[3,9]. Hydrops will develop if fetal Hb levels of <6g/dl persist for more than 4-6 days[3,9]. Those with initial Hb<5g/dl will need resuscitation at birth and emergency transfusions and will be at risk of death or major morbidities[8,9].

Some studies show that a slow rate of loss of up to 30% of the intravascular volume can be tolerated while neonates generally need NICU care if the fetal blood loss is >20ml/kg. The chance of still birth or major morbidity is significant with loss of >40ml/kg and at >80ml/kg, adverse outcomes are inevitable[3]. Therefore, FMH requires rapid, intensive and

coordinated efforts of obstetric, neonatal, transfusion medicine and the clinical laboratory[3,10].

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