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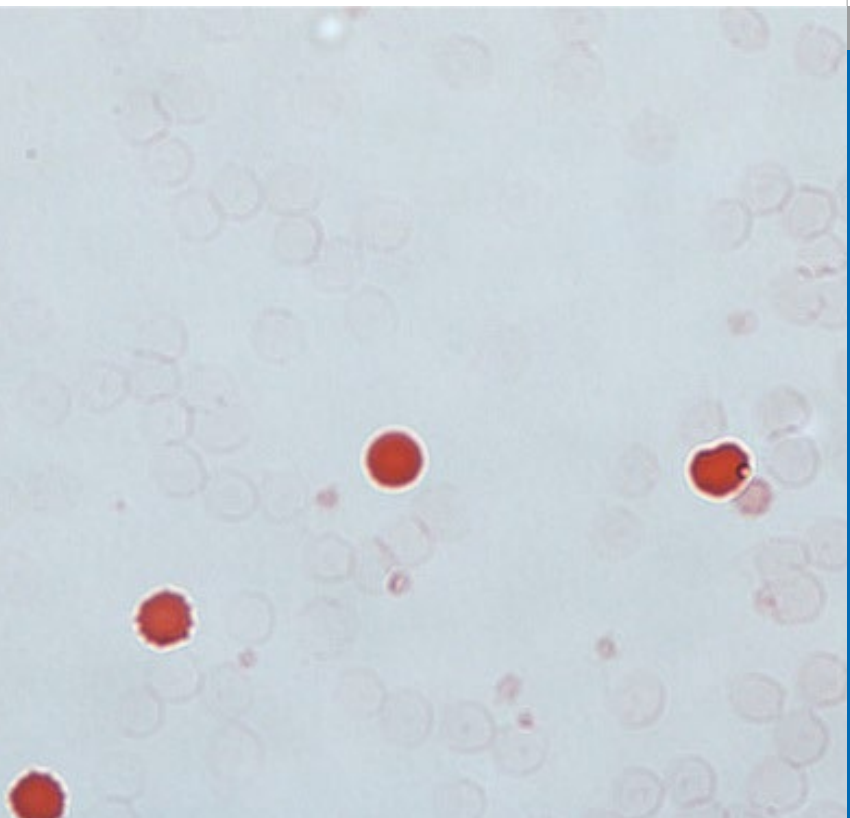
Winner of the Case of the Year Award 2004

Unexpected severe anemia in an otherwise healthy newborn



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An 18-year-old woman delivered a male infant weighing 2340 g shortly after reaching the hospital. The mother had realized that she was pregnant only two weeks prior to delivery; thus, the gestational age was unknown, and was estimated clinically to be 36 weeks according to the Dubowitz maturity assessment score.

Amniotic fluid was meconium stained, the umbilical artery pH was 7.31. Apgar scores were 7, 8 and 8 at 1, 5 and 10 minutes, respectively. The baby was breathing spontaneously and alert, but extremely pale. On examination, he had mild respiratory distress, the peripheral pulses were normal, the limbs were warm and the heart auscultation did not reveal any abnormality. Mild hepatomegaly was also present. At the age of 10 minutes, the baby had a normal blood pressure (70/36, mean 47 mmHg) and a normal arterial oxygen saturation (95%) under 30% of oxygen.

The initial blood gas analysis performed at the age of 20 minutes showed mild hypoventilation and metabolic acidosis; serum lactate was elevated (9.0 mmol/l). The differential blood count revealed severe, microcytic hypochromic anemia with a hemoglobin of 37 g/l and a hematocrit of 13 %; the erythroblasts and reticulocytes were markedly elevated (316/100 leucocytes and 291 Giga/l, respectively). Coombs' test was negative. The Kleihauer-Betke test revealed 34‰ of fetal erythrocytes in the maternal circulation, de-

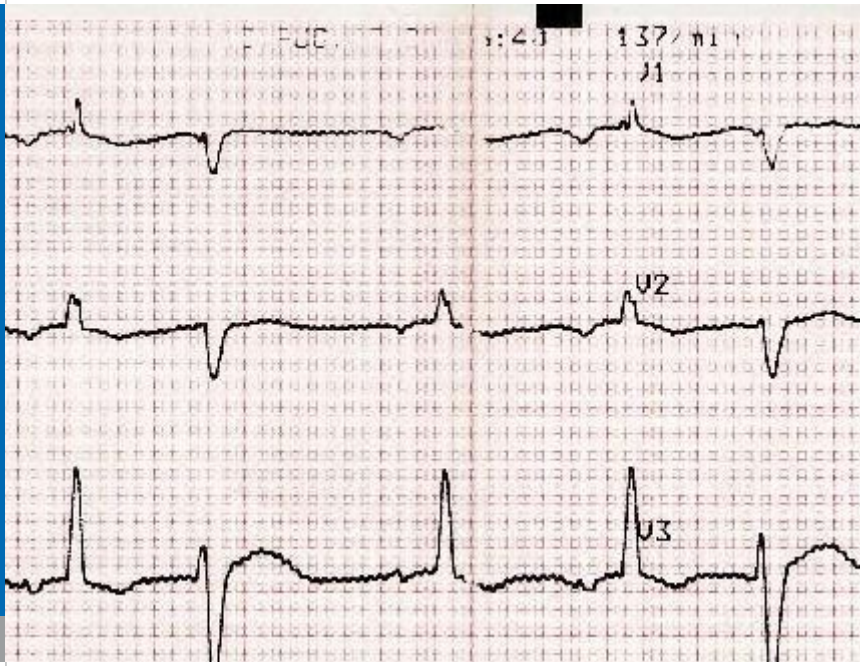

Fig. 1

ECG tracing at the age of 9 hours.

monstrating severe fetomaternal hemorrhage (FMH). The absence of hypovolemia or shock at birth, the microcytic hypochromic anaemia as well as the elevated reticulocytes and erythroblasts indicated a chronic process.

The baby was put on nasal CPAP because of respiratory distress. A total of 30 ml/kg of O Rh negative packed red blood cells was transfused over 90 minutes. Post transfusion hematocrit was 46%. However, pulmonary deterioration occurred soon after the transfusion and the oxygen requirement increased up to 90% within 30 minutes. The baby was intubated and given surfactant because surfactant deficiency could not be ruled out even though the chest X-ray showed streaky infiltrates more compatible with wet lungs. An abdominal ultrasound performed after the transfusion revealed bilateral pleural effusions and ascites. The oxygen requirement remained high under mechanical ventilation.

At the age of 9 hours, the baby developed an arrhythmia with monotopic ventricular extrasystoles, up to a trigeminus rhythm with a baseline heart rate of 70 to 80 per minute Fig. 1). Echocardiogram performed at the age of 10 hours showed normal anatomy, severe pulmonary hypertension with systemic pulmonary artery pressure, bi-directional shunt across the ductus arteriosus and the foramen ovale, and congestive heart failure. Cardiac output was less than half

of what is considered to be the lower limit of normal. Urine output was normal.

Treatment of cardiac failure was started with dobutamine. The baby showed rapid improvement with the oxygen requirement decreasing to 30% within two hours. The boy was extubated on the second day of life. The inotropes were discontinued on the fourth day of life. By the end of the first week, the baby had normal sinus rhythm with few extrasystoles, and ventricular function was nearly normal on echocardiogram.

Cerebral ultrasound scans were suggestive of asphyxia with diffuse hyperechogenicity, loss of anatomical references and slit ventricles, elevated diastolic flow velocity in the anterior cerebral artery with lowered resistance index. However, MRI performed on the 11th day of life did not reveal any changes indicating hypoxic ischemic brain damage. The clinical and neurological examination performed prior to discharge was normal. The baby was started on iron and discharged from the hospital at the age of two weeks.

This baby presented with three major symptoms: severe anemia, congestive heart failure, and mild asphyxia. In the presence of unexpected anemia at birth, the main differential diagnosis includes hemorrhage, hemolysis, and impairment of red blood cell production. The following investigations will help in making the diagnosis (1,2).

In the majority of cases, anemia is regenerative and the reticulocytes will be normal or elevated. If the reticulocytes are low, aplastic anemia may be suspected, as seen in Diamond-Blackfan or in other syndromes with impaired red cell production. In such cases, a bone marrow specimen should be obtained.

A Coombs' test is necessary and, if positive, will confirm immune-mediated hemolysis and anemia as seen with Rhesus factor, ABO, other blood group incompatibilities, or in drug-induced sensitization.

In the case of microcytic hypochromic anemia, fetomaternal hemorrhage (FMH) or twin-to-twin transfusion are the commonest diagnoses. The diagnosis of FMH will be confirmed by the Kleihauer-Betke test, which demonstrates the presence of fetal erythrocytes in maternal blood, and will help to determine how much blood was transfused into the mother. In addition, a complete blood count may show the presence of erythrocyte membrane disorders as observed in spherocytosis. If spherocytosis is suspected, an osmotic resistance test will confirm the diagnosis.

In the presence of anemia with a normal complete blood count and without hyperbilirubinemia, acute bleeding during delivery is probable. Look for obstetric complications, for external or internal (intracranial, adrenal, renal, liver, spleen, lungs) bleeding, or for DIC in case of sepsis.

Anemia with a normal blood count, hyperbilirubinemia and a negative Coombs' test is highly suspicious of non-immune hemolysis as seen in glucose-6-phosphate dehydrogenase (G6PD) and pyruvate-kinase deficiency, in some metabolic diseases, in hemoglobin defects, in congenital infections and in drug-induced hemolysis as with valproic acid. G6PD deficiency is the commonest inherited enzyme defect and has a particularly high prevalence in Africa, India, the middle east and in southern Europe.

Our baby had severe chronic FMH. The volume of fetal blood transfused into the mother was estimated to be 200 ml which is approximately the total blood volume of the baby; however, a precise estimation of the volume of FMH is difficult, because many factors influence the result of the Kleihauer-Betke test (3). The absence of signs of severe hypovolemia, the presence of microcytic hypochromic anemia, the reticulocytosis and erythroblastosis are indicative of chronic FMH. The baby developed congestive heart failure, mild hydrops and intrauterine hypoxia as the consequence of severe anemia. This was not suspected before birth, because the mother had had no regular pregnancy visits.

Retrospectively, the management of this baby was probably not adequate: the large volume of packed red blood cells transfused over a short time worsened hydrops and pre-existing heart failure, thus causing pulmonary edema and severe arrhythmias. In a baby presenting with severe anemia but no signs of hypovolemia, treatment should better consist of partial exchange transfusion with high-hematocrit blood in order to avoid fluid overload and cardiac decompensation (3). In the publication of Naulaers et al., two babies with severe neonatal anemia due to FMH were treated with a partial exchange transfusion with good success (4). Echocardiography should be performed as soon as possible in order to evaluate cardiac function. If signs of volume overload are present, inotropes and diuretics are indicated (3,4).

CONCLUSION

Mild FMH is very common. Severe FMH is rare and can lead to congestive heart failure, hydrops, and intrauterine or perinatal death (5,6). A hemoglobin concentration of less than 40 g/l is associated with a very high risk for adverse outcome, including stillbirth, neonatal death or adverse neurological outcome (3). For that reason, these infants should attend a neurological follow-up program (3,5,6).

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