In-utero blood transfusion in two etiologically – distinct anaemic fetus

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Case Presentation

Case 1

A 33-year-old Mrs. P, a multiparous woman in her fifth pregnancy (G5P2L1A2), with B positive blood group, presented at 26-27 weeks with severe non-immune fetal anemia, placentomegaly, hepatosplenomegaly and intrauterine growth restriction (IUGR). The fetus was structurally normal with no evidence of hydrops.

Her first pregnancy was terminated at 28 weeks, in view of severe IUGR with fetal anemia. The infection screen and Karyotype were normal. Further genetic work-up was not done. The second pregnancy ended with in-utero demise at 12 weeks, following the identification of bilateral pleural effusion and lymph cysts in the fetus. Testing revealed normal chromosomes. The couple had opted out of further evaluation. At 22-23 weeks, the third pregnancy was terminated in view of a similar problem (IUGR with anemia). The fourth pregnancy continued seamlessly and a term girl baby of 3.2 kg was born.

The fifth pregnancy was now under threat.

Since Rh incompatibility was not seen, the etiology of recurrent fetal anaemia was still in question. As a life-saving symptomatic measure, an in-utero transfusion was planned. The fetal haemoglobin was found to be 5 g/dl and a packed cell transfusion was done immediately at Mediscan Systems, Chennai, raising the haemoglobin to 16g/dl. At the same sitting, fetal blood was also sent for Whole exome sequencing. Following the transfusion, further follow-ups were done at our center.

At every visit, the middle cerebral artery (MCA) peak systolic velocity (an indicator of severe fetal anaemia), liquor volume, flow across portal vein and ductus venosus, and the functional assessment of fetal cardia was done diligently. Five weeks post-transfusion (Fig 1), the middle cerebral artery showed a rising trend in velocity, and the fetal heart showed signs of strain (tricuspid regurgitation).

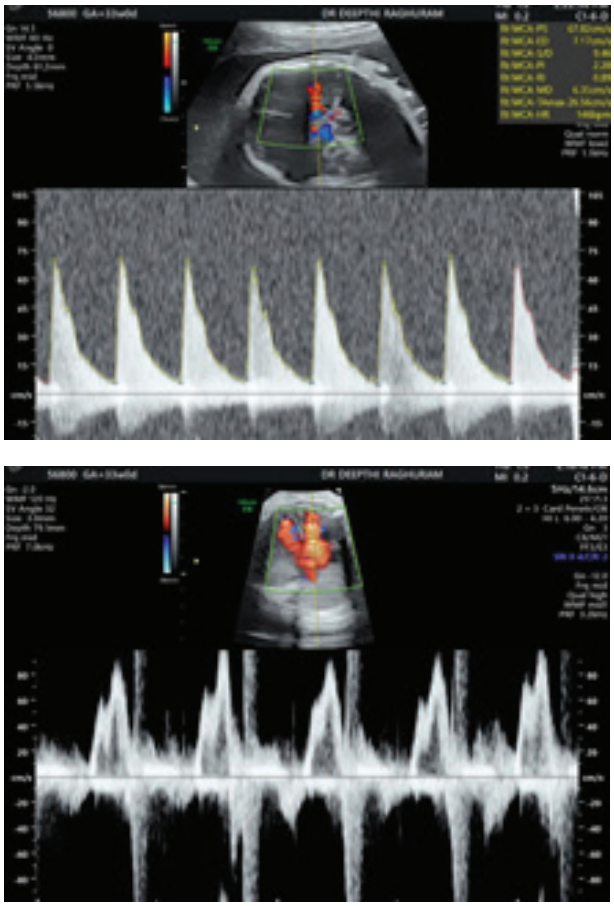


Fig (1). Middle cerebral artery peak systolic velocity >1.5 MoM suggests severe fetal anemia and severe tricuspid regurgitation implies cardiac overload.

A decision was taken to transfuse for the second time. Fetal hemoglobin was raised from 9.4 g/dl to 14.4 g/dl by transfusing double-packed O negative packed red blood cells. Soon after the procedure, the MCA peak systolic velocity dropped significantly. The fetus was evaluated by ultrasound every week.

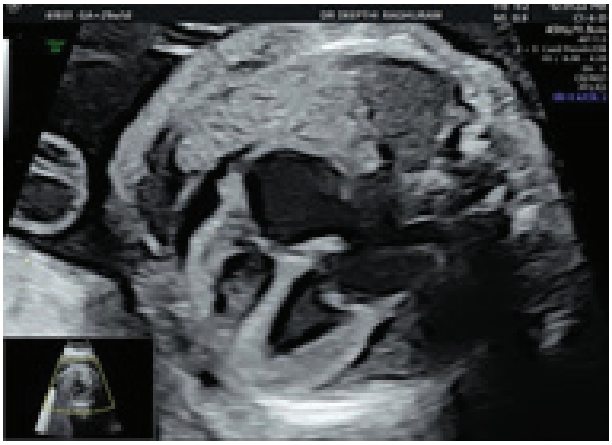
Mrs. P delivered a 3.2 kg girl baby at 36-37 weeks. The baby had jaundice, which was managed with phototherapy for a day. Thereafter, the baby was discharged on day 3 without complications. The whole exome sequencing report was normal.

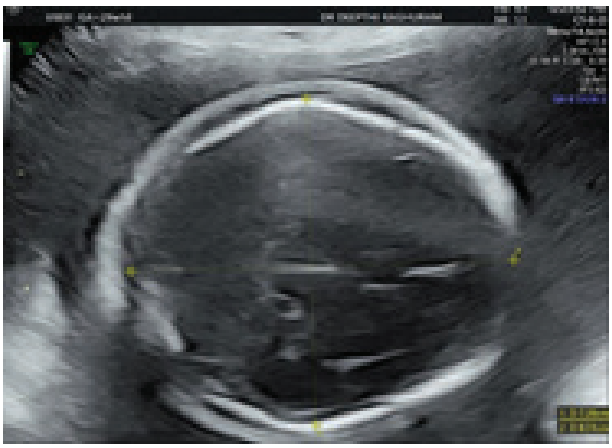
Case 2

A 32-year-old Mrs. T was referred to our unit for fetal therapy. They are a Rh - incompatible couple – The patient's blood group is B negative, Spouse's blood group is O positive. This is her sixth pregnancy (G6P4L1A1) with isoimmunisation and prior multiple fetal losses.

Her first pregnancy was 11 years ago and she delivered a healthy girl child vaginally at term. The second pregnancy miscarried at 8 weeks and surgical evacuation was done. Anti-D was given post-partum in both pregnancies. The next three pregnancies ended with in-utero demise around the 7th month, following the identification of severe anemia and polyhydramnios.

She presented to us at 29 weeks in this pregnancy with severe fetal anaemia, and features of cardiac overload such as cardiomegaly, tricuspid regurgitation, fused EA wave pattern, etc. Additionally, there was scalp edema, pericardial effusion, and ascites, suggesting fetal hydrops Fig (2).





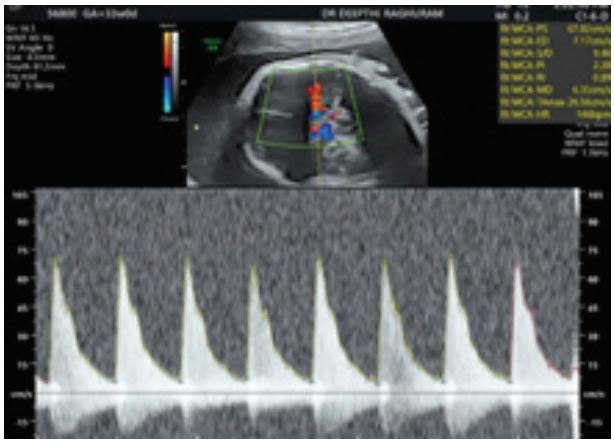


Fig (2). Cardiomegaly, pericardial effusion, scalp edema, ascites – Features of hydrops.

The patient party was counselled extensively about the implications and the need for immediate fetal therapy. O-negative packed red blood cells (PRBC) compatible with the mother's blood were immediately arranged. 130 ml of PRBC was transfused into the portal vein, which led to a rise in fetal hemoglobin from 4 to 16 g/dl. Post-transfusion, all the parameters gradually came back to normal. The fetus was monitored every week.

The average expected fall in hematocrit is 0.8%/day. Considering this drop and the features on the ultrasound, the next transfusion was planned at 33-34 weeks. As was expected, fetal hemoglobin had dropped to 8.6 g/dl at the time of the second transfusion. This was increased to 16 g/dl by transfusing 105 ml of PRBC. Both procedures proceeded uneventfully. Weekly monitoring continued until term.

Mrs. T delivered a girl baby of 2.8 kg at 36-37 weeks. Post-natal hemoglobin was 16 g/dl. The baby was under phototherapy due to neonatal jaundice for two days. No exchange or top-up transfusions were required. The baby was discharged without complications.

Discussion

Etiology of fetal anemia

Fetal anemia is a relatively uncommon but serious condition. Hydrops develops if the fetal hemoglobin falls below 5 g/dl. Immune-related anaemia i.e., RBC alloimmunization is the most common cause, followed by non-immune causes like parvovirus B19 infection, hemoglobinopathies, feto-maternal hemorrhage, etc [1].

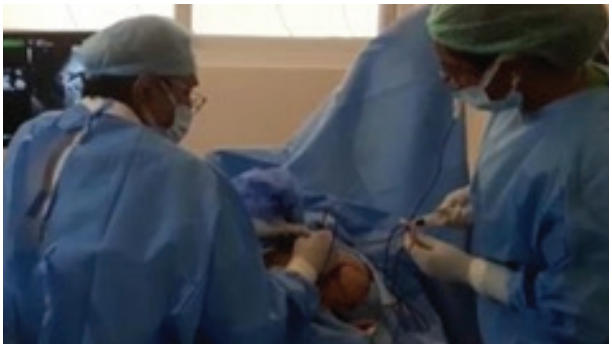
Although antenatal and postnatal administration of anti-D has become prevalent, RBC alloimmunization remains the leading cause of anemia. This could be due to unrecognized fetomaternal hemorrhage, inadequate dosage, absence of prophylaxis for other RBC antigens, or omission of Kell typing of blood transfusions for women of childbearing age.

In-utero therapy: History

In-utero blood transfusion was first attempted in 1963 by Liley [2]. The intraperitoneal route was the first approach described. However, absorption of red blood cells was inconsistent, and correction of anemia was slower, especially in hydropic fetuses. In 1981, the fetoscopic intravascular route was performed by Rodeck, which subsequently paved the way for a direct intravascular approach – the current standard of care.

Procedure

Intrauterine transfusion is done under aseptic conditions using ultrasound guidance with a 20G needle. Fetal movements are first paralyzed using intramuscular injection of muscle relaxant (Inj. Pancuronium) into the fetal deltoid. The needle is then introduced into the umbilical vein either at the placental cord insertion site or the portal vein at the site of entry into the fetal liver, depending on feasibility Fig (3).



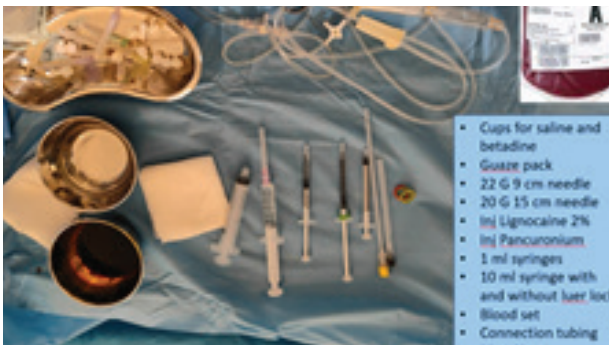


Fig (3). IUT Procedure set-up.

The blood used for transfusion is freshly prepared O-negative gamma radiated leucocyte-depleted packed red blood cells, double packed to a hematocrit of 70-80%. Transfusion aims to achieve a target hematocrit of 45-48%. The volume of blood to be transfused is determined using standard formula [3].

Intravascular transfusion (IVT) = ((target Hb – fetal Hb) × fetoplacental blood volume)/(donor Hb – target Hb);

Intraperitoneal transfusion (IPT) = (GA in weeks – 20) × 10 ml.

The anticipated fall in hemoglobin is 0.2 – 0.4 g/dl/day or hematocrit of 0.8 – 1 %/day. Repeat transfusions are planned based on the estimated decline, MCA peak systolic velocity measurements, and cardiac functional status on ultrasound.

Immediate post-procedure complications such as fetal bradycardia, prolonged bleeding after needle retraction, and uterine contractions are seen in 4-5% of cases [4]. Thus, intrauterine transfusion is an effective treatment yielding a high survival of 90% with good long-term neurodevelopmental outcomes.

Postnatal outcome

The commonest neonatal complication is jaundice. The majority of these infants can be managed with phototherapy and a limited number of top-up and exchange transfusions5. Parvovirus-related anemia also has excellent neonatal outcomes.

Early identification of fetal anemia and appropriate therapy improves perinatal outcomes, especially in non-hydropic fetuses. With regards to long-term neurodevelopmental outcomes, the incidence of impairment in antenatally treated fetuses is low (4.8%). Prevention of fetal hydrops further improves the long-term outcome[6].

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