

Intrauterine fetal transfusion

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ABSTRACT

The incidence of perinatal death resulting from rhesus (Rh) isoimmunization has dropped dramatically since the introduction of Rh immunoglobulin. However, Rh sensitization continues to be one of the leading causes of fetal anemia. Our patient is a 38-year-old woman; she gives a history of 2 uneventful pregnancies followed by 5 consecutive stillbirths. Investigations revealed an anti-D titre of 1/2048 and anti-C titre of 1/256. Ultrasound examination revealed fetal ascites at 18 weeks gestation. The fetus had a total of 9 successful intrauterine transfusions. She was delivered by an elective cesarean section at 34 weeks gestation; outcome was a healthy female baby weighing 2060g. Examination at 9 month of age showed normal growth and neurodevelopment.

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Following the introduction of rhesus (Rh)-D immunoglobulin, the incidence of neonatal death due to RhD hemolytic disease dropped dramatically. However, anti-D antibodies still remain an important cause of fetal hemolytic anemia. Maternal sensitization can occur resulting from failure to administer anti-D immunoglobulin, leakage of fetal blood into the maternal circulation during the third trimester and excessive fetomaternal hemorrhage not neutralized by standard anti-D immunoglobulin dose.¹ Antenatal administration of prophylactic Rh-D immunoglobulin reduces the risk of sensitization from 1.5-0.2%.² However, the cost benefit of such policy remains unclear.³ Our objective is to report the management of a case Rh isoimmunization managed successfully by uterine blood transfusion.

Case Report. A 39-year-old expatriate woman was referred to the Maternal Fetal unit in Al-Ain Hospital at 17 weeks gestation for high Anti-D titre and Anti-C titre and bad obstetrical history. Her blood group was reported as "A" Rh negative. She was gravida 8, para 2, with history of 5 stillbirths. Her first 2 pregnancies were 16 and 14 years ago.

Both were uneventful and were delivered vaginally at term. Both babies were females of average weight. Anti-D immunoglobulin was not administered post delivery. This was followed by 5 stillbirths. The first stillbirth was near term and the last was at 24 weeks gestation. At delivery babies were edematous with no obvious structural abnormalities. On referral the Anti-D titre was 1/2048 and Anti-C titre was 1/256. Ultrasound examination confirmed her dates, and no structural abnormalities were detected. The estimated fetal weight (EFW) was 295 grams. No fetal ascites was detected. The middle cerebral artery peak systolic velocity (MCA PSV) was 55 cm/s, umbilical vein maximum flow velocity (UVV_{max}) velocity was 17 cm/s and liver length was 18mm. The MCA PSV was above the 90th percentile for 17 weeks gestation. The UVV_{max} and liver length were within normal values. A follow-up ultrasound examination one week later revealed moderate fetal ascites. The MCA PSV was 58 cm/s, the UVV_{max} and liver length remained within normal values. After proper counseling the patient was prepared for cordocentesis and intrauterine transfusion (IUT) the following morning. The IUT was performed through

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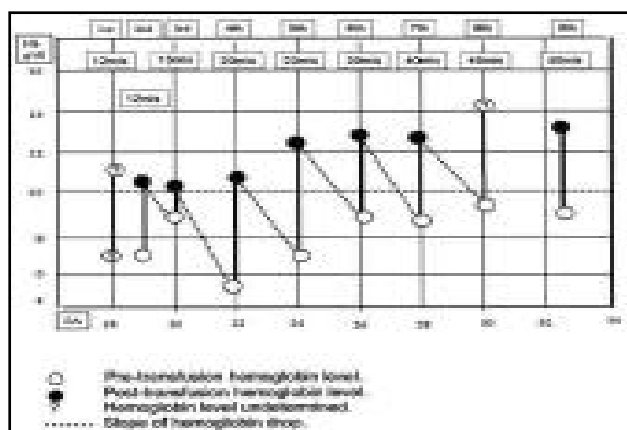


Figure 1 - Details of the 9 intrauterine transfusions.

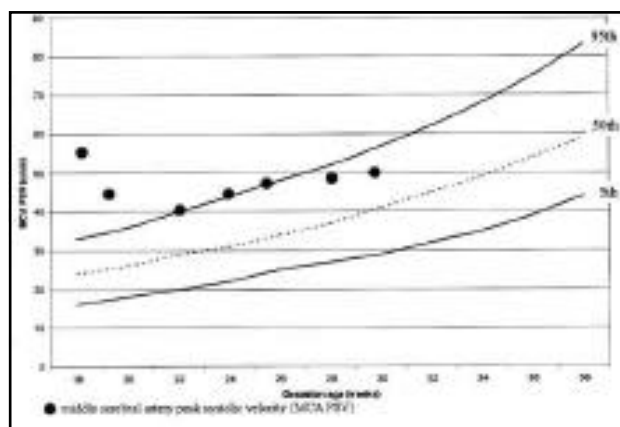


Figure 2 - Changes in the middle cerebral artery peak systolic velocity associated with intrauterine transfusions.

the umbilical vein at its placenta root. Unfortunately, both pre and post-transfusion blood sample were clotted and hemoglobin levels were undetermined. A total of 12ml of "O" Rh negative blood was transfused. The second transfusion was 5 days later. The pre-transfusion hemoglobin was 6.5g/dl, and 12ml of blood was transfused. The post-transfusion was 10.3g/dl. Subsequent transfusions were performed through the hepatic portion of the umbilical vein (intrahepatic vein). Her last transfusion was at 33+4 weeks gestation. The fetal post-transfusion was 13.1g/dl. **Figure 1** shows the detail of the 9 transfusions. The MCA PSV gradually dropped to normal values as the hemoglobin level returned to normal (**Figure 2**).

The mother had an elective cesarean section at 34 weeks gestation. The decision for cesarean section was mainly for the bad obstetrical history. A female baby of 2060g was delivered with Apgar score of 6 and 8 at one and 5 minutes and was transferred to the special care baby unit. She was well with no abnormal features. The head circumference measured 31.5cm (50th percentile), her length was 45cm (>50th and <90th percentile) and she weighed 2060g (50th percentile). The liver was palpable 3.5cm below the costal margin; no other abnormal findings were detected. Her hemoglobin level was 14.4g/dl, reticulocytic count was 0.2% bilirubin (unconjugated) level was 4.9mg/l and direct Coombs test was negative. She was kept under phototherapy for 7 days. The baby was discharged on day 25 in good health. Her weight on discharge was 2289g, and hemoglobin level was 8.9g/dl. At the age of 38 days her hemoglobin dropped to 5.8g/dl, she was admitted to hospital and received blood transfusion. Her last follow-up visit was at 9 months of age. Both her growth and neurodevelopment assessment were reported as normal. Her body measurements were within normal, the head circumference was 44cm, body

length was 70cm and her weight was 10kg. She was able to sit unsupported and was able to makes 2-syllabled sounds.

Discussion. The presence of multiple maternal antibodies significantly increases the severity of fetal anemia and need for intrauterine fetal transfusion.⁴ Our patient had high titers for 2 antibodies (anti-D titer 1/2048 and anti-C titer 1/256). This was resulting from failure to administer anti-D immunoglobulin following her first 2 deliveries. These high maternal antibodies levels led to the severe anemia, early hydrops and poor pregnancy outcome. Hemolytic anemia due to anti-C is of lesser severity than that of anti-D, and rarely associated with perinatal death.⁵

Fetal blood sampling is considered the gold standard test for the diagnosis of fetal anemia.⁶ However, this procedure carries a risk of fetal loss of 1.4%.⁷ To avoid unnecessary fetal loss, the correct timing for cordocentesis and intrauterine transfusion is crucial. The MCA PSV has a high sensitivity and specificity for the prediction of fetal anemia compared to other non-invasive tests such as the UVV_{max} , liver length and spleen perimeter.⁸ This was evident in our case; the MCA PSV abnormality preceded fetal ascites, whereas both UVV_{max} and liver length measurements remained within normal values in the presence of fetal ascites and severe anemia.

The perinatal survival rate following intrauterine transfusion is approximately 90%, this is reduced by 25% in the presence of fetal hydrops.⁹ The risk of severe anemia before 22 weeks gestation is approximately 3/100,000. The survival rate for these fetuses can be as low as 55%.¹⁰ The risk for fetal loss in our case was high, the fetus was hydropic at 18 weeks gestation and required 9 intrauterine transfusions. The initial 2 transfusions were

performed through the placental root. However, with uterine growth and the placenta pushed posteriorly the placental root was no longer accessible. The hepatic portion of the umbilical vein was used for subsequent transfusions.

Reports on the neurodevelopment and growth of infants who had intrauterine transfusions are reassuring; normal developmental outcome can be expected. However, there are some reports of increase risk of hearing impairment.¹¹ Growth and neurodevelopment assessment of our reported case at 9 months of age was reported as normal. The development of Maternal Fetal services will provide an important option for mothers with similar problems, and other conditions requiring intrauterine intervention.

References

1. Mayne S, Parker JH, Harden TA, Dodds SD, Beale JA. Rate of RhD sensitisation before and after implementation of a community based antenatal prophylaxis programme. *BMJ* 1997; 315: 1588.
2. Crowther CA, Keirse MJ. Anti-D administration in pregnancy for preventing rhesus alloimmunisation. *Cochrane Database Syst Rev* 2000; CD000020.
3. Bowman J. Thirty-five years of Rh prophylaxis. *Transfusion* 2003; 43: 1661-1666.
4. Spong CY, Porter AE, Queenan JT. Management of isoimmunization in the presence of multiple maternal antibodies. *Am J Obstet Gynecol* 2001; 185: 481-484.
5. Bowman JM, Pollock JM, Manning FA, Harman CR. Severe anti-C hemolytic disease of the newborn. *Am J Obstet Gynecol* 1992; 166: 1239-1243.
6. Ryan G, Morrow RJ. Fetal blood transfusion. *Clin Perinatol* 1994; 21: 573-589.
7. Ghidini A, Sepulveda W, Lockwood CJ, Romero R. Complications of fetal blood sampling. *Am J Obstet Gynecol* 1993; 168: 1339-1344.
8. Dukler D, Oepkes D, Seaward G, Windrim R, Ryan G. Noninvasive tests to predict fetal anemia: a study comparing Doppler and ultrasound parameters. *Am J Obstet Gynecol* 2003; 188: 1310-1314.
9. Moise KJ Jr. Management of rhesus alloimmunization in pregnancy. *Obstet Gynecol* 2002; 100: 600-611.
10. Poissonier MH, Picone O, Brossard Y, Lepercq J. Intravenous fetal exchange transfusion before 22 weeks of gestation in early and severe red cell fetomaternal alloimmunization. *Fetal Diagn Ther* 2003; 18: 467-461.
11. Hudon L, Moise KJ Jr, Hegemier SE, Hill RM, Moise AA, Smith EO et al. Long-term neurodevelopmental outcome after intrauterine transfusion for the treatment of fetal hemolytic disease. *Am J Obstet Gynecol* 1998; 179: 853-863.