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CASE REPORT

Successful Management of Early Onset Rh-immunized Pregnancy

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ABSTRACT

Rh-isoimmunization still remains an important preventable cause of perinatal mortality and morbidity. The improved perinatal outcome in sensitized patients is mainly attributed to application of color Doppler ultrasonography as a noninvasive method of detecting and monitoring fetal anemia and fetal well-being, improvement in ultrasonography machines and fetal interventional techniques and better neonatal intensive care facilities. Here, we present a case G3P2L1D, Rh negative with previous lower segment cesarean section (LSCS), diagnosed to be indirect Coomb's test (ICT) positive (1:64) at 9 weeks.

She was followed up with serial ICT titers every 2 weeks along with ultrasonography (USG) and Doppler. Fetal anemia was detected with middle cerebral artery (MCA) Doppler at 27 weeks and same treated with intrauterine transfusions twice. She was diagnosed to have gestational diabetes mellitus and treated for the same. Patient then delivered at 36 weeks and 5 days by emergency LSCS in labor, a healthy girl baby, 3.07 Kg. Postnatally, baby developed jaundice and was treated with double light phototherapy. Baby also developed anemia subsequently 3 days after birth and was treated with one dose of intravenous (IV) immunoglobulin. Baby with mother were discharged on postoperative day 5 in good health.

Keywords: Indirect Coombs test, Intrauterine transfusion, Middle cerebral artery Doppler study, Rh immunization.

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INTRODUCTION

The incidence of Rh-isoimmunization has reduced worldwide due to increased awareness and implementation of antepartum and postpartum prophylaxis. It is estimated that only about 16 to 17% of RhD-negative women who deliver a Rh positive fetus will become alloimmunized if not administered anti-D immunoglobulin. The development of anti-D antibodies usually occurs as a result of fetomaternal hemorrhage (FMH)/sensitization from previous pregnancy in an RhD-negative woman with an RhD-positive fetus. The transport of these maternal antibodies, from the placenta to the fetus subsequently destroys fetal red blood cells—resulting in fetal anemia. The early detection of fetal anemia is the most important point in the treatment of immune hydrops fetalis. Previously invasive techniques, such as amniocentesis and cordocentesis, were used to identify fetuses with hyperbilirubinemia and severe anemia. Marie et al reported that middle cerebral arterial peak systolic velocity middle cerebral artery—peak systolic velocity (MCA-PSV) value detected by Doppler ultrasonography increases in fetuses with anemia and is now the mainstay in noninvasive diagnosis of fetal anemia.[1]

Intrauterine management of fetal anemia is mainly by intrauterine transfusions.

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CASE REPORT

A 26 years old, gravida 3 para 2, live 1, death 1, registered with us from 9 weeks, with Rh negative complicating pregnancy. Indirect Coomb's test (ICT) done at 1st visit 9 weeks (1:64) was positive.

Her obstetric history is 1st pregnancy (2009)—full term normal delivery, girl, 3.4 kg, anti-D given, alive and healthy. 2nd pregnancy—in 2011 full term LSCS (infetal distress), boy, 3.3 kg, neonatal death on D2 of life. Patient has no records of baby's blood group, ICT status, postnatal anti-D administration. 3rd pregnancy—2013 present pregnancy.

As the patient was ICT positive, she was followed up with serial ICT titers (once in 4 weeks) and fetal MCA Doppler studies from 20 weeks to detect the presence of fetal anemia.

INDIRECT COOMB'S TEST TITERS

Nine weeks—1:64; 13 weeks—1:512; 20 weeks—1:512; 26 weeks—1:256; 30 weeks—1:256—at 13 weeks nuchal thickness (NT) scan done and same found to be normal. At 20 weeks, anomalies were ruled out. Evidence of

fetal anemia was first seen at 28 weeks (MCA-PSV—1.6 MOM) (Table 1). Hence, the 1st intrauterine transfusion was given.

Patient was given injection betamethasone, two doses, 24 hours apart at 29 weeks. Patient was then serially followed with MCA Dopplers. At 33 weeks (MCA-PSV) increased to 1.6 MOM. Hence, 2nd transfusion was done. Prior and post-transfusion MCA Doppler and hemoglobin values were noted (Table 2). After 32 weeks, pregnancy was followed with growth scans, and fetal well-being tests nonstress test (NST). Patient was diagnosed to have gestational diabetes mellitus (GDM) at 30 weeks; hence, started on metformin 500 mg od and injection mixtard 6U HS. As patient went into labor, decided for emergency LSCS (in view of previous LSCS with mobile head in labor) at 36 weeks. She delivered a healthy girl baby—3.07 kg.

Serum bilirubin was monitored Q 6th hourly and found to be in the increasing trend (8.9, 12.2, 11.9, 11.4, 9.8) (Table 3).

Baby was started on double light phototherapy. Baby had drop in Hb levels (14.3, 13.6, 11.8, 12.3, 11.5), after birth which was closely monitored. Same stabilized after 5 days of birth.

Septic work up done and cultures were found to be negative. Baby was given one dose of IV immunoglobulins in view of high bilirubin levels. On day 4 to 5, bilirubin levels were decreasing and hence phototherapy was stopped. Baby and mother were discharged on POD.[5]

DISCUSSION

Prevention of Rh-isoimmunization should be advocated by determination of blood type and an antibody screen at the first visit.

It is estimated that only 16 to 17% of RhD-negative women who deliver a Rh-positive fetus will become alloimmunized if not administered anti-D immunoglobulin.[2] According to ACOG, all Rh-negative, nonsensitised pregnant women should receive 300 mcg of RhIG at 28 weeks.

This is sufficient to protect from sensitization due to FMH of 30 ml of fetal whole blood. Within 72 hours for Rh positive birth, conditions leading to potential FMH are spontaneous abortion, threatened abortion, ectopic pregnancy, hydatiform mole, amniocentesis, chorionic villus sampling, fetal blood sampling, suspected abruption, placenta previa with bleeding, external cephalic version, within 72 hours of Rh-positive infant.

Early detection of fetal anemia is accepted as the first and effective step in management of fetuses affected with Rh isoimmunization. Though amniocentesis and cordocentesis have been used for the past 40 and 16 years respectively, both these procedures are invasive and related with risks to the fetus. It has now been outdated with the advent of MCA-PSV Doppler, which is now being used widely as the main noninvasive modality in the detection of fetal anemia. An anemic fetus will have a raised MCA-PSV due to increased blood flow to the brain due to the high output state and the reduced viscosity. It has been seen that MCA-PSV values of greater than 1.5 MOM in fetuses with anemia require fetal intrauterine transfusion. Middle cerebral arterial-peak systolic velocity has sensitivity of 74% with 10% false positive rate for prediction of severe and moderate anemia. It has been reported that in fetuses previously transfused once, timing of the second transfusion can be determined noninvasively by Doppler ultrasonography on a basis of increased peak velocity of systolic blood flow in the middle cerebral artery. Also, the decrease in MCA-PSV Doppler just after intrauterine transfusion in anemic fetuses shows quick response of the fetus to correction of anemia.[1,2] The management of fetal anemia differs with gestational age of the patient. If greater than 34 weeks, termination of pregnancy is the treatment of choice. If less than 34 weeks, intrauterine transfusion (IUT) is the treatment of choice.

Before the intervention of intrauterine fetal transfusions, Rh-sensitized fetuses were routinely delivered at the 32nd week of gestation.[3]

Table 1: Middle cerebral arterial Doppler study and GA

Date	*GA*	*MCA Doppler*
6/6/13	20 weeks + 5D	0.95 MOM
20/6/13	22 weeks + 5D	1.05 MOM
12/7/13	25 weeks + 6D	1.21 MOM
22/7/13	27 weeks + 2D	1.57 MOM
26/7/13	27 weeks + 6D	1.61 MOM
13/8/13	30 weeks + 3D	1.4 MOM
2/9/13	33 week + 2D	1.6 MOM

MOM: Multiple of median; GA: Gestational age

Table 2: Pre- and post-transfusion MCA and Hb values

Gestational age	*Transfusion given*	*Pretransfusion MCA-PSV*	*Post-transfusion MCA-PSV*	*Pretransfusion Hb gm%*	*Post-transfusion Hb gm%*
28 weeks	85 ml of O Neg PC, through portal vein	1.6 MOM	0.89 MOM	8.3	17
32 weeks and 3 days	130 ml of O Neg PC, through portal vein	1.61 MOM	1.00 MOM	8.2	23

MOM: Multiple of median

Table 3: Postnatal bilirubin and Hb

Day	*1*	*2*	*3*	*4*	*5*
T. bilirubin (mg)	8.9	12.2	11.9	11.4	9.8
D. bilirubin (mg)	1.12	1.71	1.64	1.53	1.2
Hb (gm)	14.3	13.6	11.8	12.3	11.5

Intrauterine transfusion has now reduced the number of complications, such as prematurity, hyaline membrane disease, exchange transfusions and prolonged neonatal intensive care facilities.

In hydropic babies after intrauterine transfusions, reversal rate varied between 39 and 88% indicating a guarded prognosis even after intervention. Thus, prophylactic intrauterine transfusion done as early as 15 weeks before hydropic features become evident, can be life saving in fetuses of severely Rh-sensitized mothers.[4]

Intrauterine transfusion is a milestone interventional procedure, and is life saving in Rh-sensitized pregnancies with elevated color Doppler indices.[5,6] Fetal intrauterine transfusions are the mainstay of fetal therapy with an overall perinatal survival of greater than 85%.[7,8]

Neonatal management of fetal anemia due to Rh-isoimmunization includes phototherapy, IV immunoglobulins and exchange transfusion. Intravenous immunoglobulins administration to neonate with Rh isoimmunization has been associated with reduction in requirement of exchange transfusion.[9]

CONCLUSION

Successful management of Rh-negative immunized pregnancies is possible with utilization of serial MCA Doppler study (noninvasive) for detecting fetal anemia and timely management with intrauterine transfusion.

Postnatal administration of IV immunoglobulins avoids requirement of exchange transfusion.

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