

Case report:

Rh-D-primigravida mother with anti Rh-17 antibodies causing mild haemolytic disease of foetus and newborn in baby: a case report

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Abstract

Rh-D- is an unusual phenotype in Rh blood group system, lacking all Cc or Ee antigens but demonstrates a stronger D antigen expression. We describe here an extremely rare Rh-D phenotyped mother with first baby affected by haemolytic disease of foetus and newborn (HDFN). A 20-year-old pregnant lady, presented in active labour with foetal distress and planned for emergency cesarean section. Her blood group was A RhD positive, with positive antibody screening. Antibody identification demonstrated multiple antibodies against RhCc Ee polypeptide by the reference laboratory. Rh phenotype was -D-/-D- with no C/c and E/e antigen but strong D antigen. Crossmatch was incompatible with all A RhD positive units. Management of such patient is extremely difficult due to the scarcity of Rh-D- donor blood. In this case, reference laboratory had one frozen Rh-D- blood ready for use if indicated. Fortunately, patient underwent caesarean section without any complication. Baby was grouped as A Rh-D positive with probable Rh genotype as CDe/-D-. Baby's DCT was positive and eluate showed antibodies of identical reactivity as mother. Baby developed mild jaundice at day-2 and managed with phototherapy. Clinically Rh-D- phenotype in pregnant women can cause mild to fatal HDFN. Routine antibody screening in pregnant women can detect such rare case that helps proper management of mother and baby. Prior arrangement of this rare blood is warranted to prevent the maternal and infant mortality and morbidity.

Keywords: Rh-D-phenotype; primigravida; HDFN; alloantibody

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Introduction

The Rh blood group is one of the highly immunogenic and complex blood group systems, important in both transfusion medicine and pregnancy. Here, two closely linked genes located on chromosome-1 control the expression of the Rh antigens. RHD gene codes for the D polypeptides while RHCE gene determines the C, c, E, e antigens¹. Red blood cell alloimmunization against Rh antigen can occur following sensitization by pregnancy or blood

transfusion resulting in haemolytic transfusion reaction (HTR) and haemolytic disease of foetus and newborn (HDFN)². Rh-D- phenotype (Rh17) is one of the rare phenotype in the Rh blood group system that lacks all Rh antigens except D³. It was first described in 1950, showed absence of C/ c and E/ e antigens and strong D antigen expression on the surface of red blood cells⁴. The genetic events for the Rh-D phenotype are not well-defined but it may be due to homologous deletion of the RHCE genes and

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recombination of portions of the RhD gene with the RhCE gene causing overexpression of RhD antigen⁵. The frequency of -D- haplotype ranges from 0.0005 in Sweden, 0.0032 in Japan and 0.0047 in Iceland⁶.

Rh-D- phenotyped individuals are highly susceptible to sensitization to Rh antigen by immune stimulus like transfusion or pregnancy to produce a variety of Rh antibodies against C, c, E or e antigens known as anti-Rh17. Most of the Rh-D- individuals showed presence of anti-Rh17 antibodies in their serum that reacts as a single specificity^{4,7}. This antibody is best detected with antiglobulin testing, and reacts with both normal and enzyme-treated red blood cells⁵. This clinically significant antibody can produce severe HTR or mild to severe HDFN⁴. For transfusion in a patient with anti-Rh17 antibody, blood products must be compatible Rh-D- phenotype or Rh null red blood cells^{5,8}. Management of these patients is particularly difficult due to the scarcity of antigen-negative blood for transfusion. There is no data on the prevalence of Rh-D- phenotype in Malaysia. In this case report, we are presenting an extremely rare Rh-D- phenotype in a primigravida patient having first baby affected with HDFN due to Anti-Rh 17. We hope, this case report may add knowledge to the current understanding of Rh-D- phenotype in Malaysia and its management in emergency situation.

Case Report

A 20-year-old Myanmar lady, primigravida, at 40 weeks of gestation admitted at latent phase of labour in our hospital. Her pre-transfusion test was done as the patient was planned for emergency lower segment cesarean section (LSCS) due to foetal distress. Subsequently she delivered a baby girl with Apgar scores of 8 and 9 at 1 and 5 minutes, respectively. However, the baby developed neonatal jaundice on day-2 of life and early onset of pneumonia.

The laboratory test performed on mother during pre-transfusion testing showed her blood group as A RhD positive with positive red cell antibody screening with all three cell panel (Bio-Rad ID-Dia Cell I-II-III Asia). Full antibody investigation was proceeded. Her probable Rh Genotype was determined as -D-/-D-(D17) showing no C/c and E/e antigen reactivity but strong D antigen expression. Direct antiglobulin test (ID-Card“LISS/Coombs”) and autocontrol was negative. Antibody identification

using LISS and papain treated panels (11 cell panel, Bio-Rad ID DiaPanel, ID DiaPanel-P, gel technique) demonstrated strong positive reactions with all cells. Crossmatching was incompatible (Gel technique) with all A RhD positive donor cell. Due to rare Rh-D- phenotype in the patient, antibodies against the high prevalence antigens of the RhCcEe polypeptide was suspected. Patient's sample was send to reference laboratory, National Blood Centre Malaysia for antibody identification and confirmed the presence of antibody against RhCcEe polypeptide. The management of such patient is extremely difficult due to the scarcity of Rh-D- phenotyped donor blood. The primary team under the obstetrician was informed about this rare blood group. In this case, the reference laboratory had one unit of frozen Rh-D- phenotyped blood ready for use if indicated. We maintained a good communication between the obstetric colleagues, blood bank personnel and reference laboratory personnel about the patient's status. Fortunately, patient underwent LSCS without any complication with underlying haemoglobin of 13g/dl and therefore blood unit was not used.

Baby's sample was send for investigation. Blood group was A RhD positive and probable Rh genotype as CDe/-D-. Direct antiglobulin test was positive with anti-IgG type and red cell eluate showed multiple antibodies of identical reactivity as the mother. Baby's G6PD was normal. The haemoglobin and haematocrit were 12.4 g/dl and 38.1%, respectively, white cell count $9.3 \times 10^9/L$, platelet count $261 \times 10^9/L$, and reticulocytic count $8.1 \times 10^9/L$. Total bilirubin concentration was 134.1 $\mu\text{mol/l}$ with normal range of (3.4 - 20.5 $\mu\text{mol/l}$). Direct bilirubin was 7.6 $\mu\text{mol/l}$ (reference range is 0-8.6 $\mu\text{mol/l}$). The baby was diagnosed as having mild HDFN secondary to maternal anti-Rh17. Baby was managed with phototherapy. On discharge at day-5, baby was stable, tolerating breast feeding well and vital signs were stable.

In view of this rare phenotype, the patient and her husband were counseled about this rare phenotype. Patient was asked to bring her immediate family members for screening of the Rh phenotype, however, they failed to come for screening and lost to follow up to the hospital.

Discussion

This case illustrates an unusual Rh-D- phenotype

with presence of alloantibody against high-frequency antigens RhCcEe polypeptide (anti Rh17). Although she was under antenatal follow up with a maternity clinic, red cell antibody screening was not performed. During delivery, patient admitted to our hospital and this rare phenotype was identified with presence of alloantibody. Patient denied any history of blood transfusion or abortion. In this present case, probably she was immunized during current pregnancy or undiagnosed previous spontaneous abortion and developed allo-antibodies against Rh CcEe antigens as these antigens are absent in her plasma. Here, one important finding is that her first baby was affected. It has been mentioned that the first baby may be affected in a -D-/-D- woman⁹. Therefore, preventive measures must be emphasized from first pregnancy during the follow up. In this present case, although patient was on antenatal follow up, red cell antibody screening was not performed as this is not a common practice for the RhD positive mothers. Therefore, patient's red cell antibody status and Rh phenotype status remain undetected before labour. We suggest antibody screening for all pregnant lady irrespective of RhD positive or negative status of the patient.

Management of such patient is extremely difficult due to the limited availability of such rare -D-phenotyped donor blood. In the absence of inventory or database for such rare donors in any local blood bank, it is almost impossible to find compatible blood¹⁰. In this present case, our reference laboratory had one unit of frozen Rh-D- phenotyped blood ready for use if indicated and a good communication was continued among all teams about the patient's status. Fortunately, patient underwent caesarean-section without any complication and did not require any transfusion. On the other hand, the baby although presented with neonatal jaundice, managed with phototherapy alone. However in the subsequent pregnancies, the antibody titer may rise enough to cause moderate to severe HDFN and may require special investigations to monitor the baby and perhaps require intrauterine transfusion. Therefore, in subsequent pregnancies of such cases, the patient should be followed up regularly with appropriate investigations to monitor the mother and the foetus; and mother's condition should be updated regularly to the reference lab in order to keep the compatible blood ready for use. The neonatologist should also

be consulted to monitor the HDFN after delivery. A number of cases of such rare Rh-D- phenotype with antibodies causing moderate to severe HDFN were reported indicating the clinical significance of this antibody in pregnancy^{7,11,12,13,14}

In the management of such rare phenotyped patients, a few options are available to replace the blood transfusion. Initiation of iron therapy and erythropoietin therapy at a suitable dose can increase the haemoglobin and minimize the need for transfusion⁷. Family screening among first degree relatives to search the phenotype specific blood is also indicated in such rare case in order to get the compatible phenotype specific blood⁵. It is also mentioned that the alloantibody levels can be lowered with plasma exchange in post conception period, however this method is not of much success¹⁰. Any additional blood loss must be prevented including restricting the number and volume of blood draws during sample collection. In case of elective surgery, iron therapy with preoperative autologous collection as well as use of intraoperative red cell salvage and autologous/ allogeneic frozen red cell units are the good options available^{1,5}.

For the management of severe HDFN, baby may need intrauterine transfusion (IUT), exchange transfusion (ET), or neonatal top-up transfusions. In such cases, serial maternal blood donations followed by washing and irradiation are the best choices. Mother may be advised to take iron and folic acid supplementation or recombinant human erythropoietin and intravenous iron for the prevention of anaemia. It is mentioned that for foetal transfusion therapy, even ABO incompatible maternal blood are a good option because the fetus does not have its own anti-A and anti-B antibodies, so maternal red cells would not be hemolyzed¹⁴. For ET, ABO compatible maternal blood with the cord blood may be the best option if mother can tolerate blood donation¹. Other options for foetal IUT or ET are Rh-D-phenotype matched blood from mother's sibling or frozen rare Rh-D- donor blood^{4,10,11,13}. Use of intravenous immunoglobulins (IVIg) are reported to be successful to inhibit haemolysis before and after exchange transfusion⁷ and found that if started weekly at the end of the first trimester can delay the IUT for up to 25 days¹.

Conclusion

This case report demonstrates an extremely rare

Rh-D- phenotype detected in a primigravida patient during labour with first baby affected by HDFN due to anti Rh 17. Increased awareness about this antibody is necessary and early detection of such rare cases may help to arrange the rare blood and thus prevent the maternal and infant morbidity. A combined multidisciplinary approach including transfusion medicine specialist, obstetrician, and neonatologist is necessary in order to manage such cases. Routine antibody screening in all pregnant women despite their Rh blood group status is a must do thing to detect such rare antibody.

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