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Case Report

Hemolytic disease of the newborn due to minor blood group incompatibility: Sibling cases

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Abstract

Hemolytic disease of the newborn is mostly caused by the hemolysis of fetal erythrocytes by maternal and placental antibodies. Antigens in this group are Kell, Duffy, Kidd, MNSs and the E, e, C, c found in the Rh system. They are responsible for 3-5% of hemolytic disease of the newborn. In cases of minor blood group incompatibility, clinical picture may vary from subclinical hemolysis findings to active hemolysis and from blood clotting to neonatal jaundice. Here we present two sibling cases with multiple minor blood group (c, Kell, Cw) incompatibilities of whom the first one was diagnosed two years ago as glucose 6-phosphate dehydrogenase deficiency and undergone exchange transfusion and ultimately diagnosed as minor blood group incompatibility after the diagnosis of the second sibling.

Keywords: Hemolytic disease; minor blood group incompatibility; newborn.

INTRODUCTION

Hemolytic disease of the newborn is mostly caused by the hemolysis of fetal erythrocytes by maternal and placental antibodies. Hemolytic anemia and indirect hyperbilirubinemia due to Rh sensitization, which has been frequently seen in the past years, has been reduced by the widespread use of anti-D gamma globulin and the rate of minor blood group incompatibilities has increased gradually in etiology (1). Antigens in this group are Kell, Duffy, Kidd, MNSs and the E, e, C, c found in the Rh system. They are responsible for 3-5% of hemolytic disease of the newborn. In cases of minor blood group incompatibility, clinical picture may vary from subclinical hemolysis findings to active hemolysis and from blood clotting to neonatal jaundice (2,3). Here we present two sibling cases with multiple minor blood group (c, Kell, Cw) incompatibilities of whom the first one was diagnosed two years ago as glucose 6-phosphate dehydrogenase (G6PD) deficiency and undergone exchange transfusion and ultimately diagnosed as minor blood group incompatibility after the diagnosis of the second sibling.

CASE REPORTS

CASE 1

A 24-year-old G2 / P2 / A0 mother delivered a 3000 g female baby with cesarean section at 37 weeks' gestation with an, Apgar score of 9 at the first minute and 10 at the fifth minute in another hospital. No postnatal problem was reported and she was discharged home on the second day of life. She was admitted to pediatric emergency department with poor sucking, a weight loss of 5.7% (2830 gr) and jaundice on postnatal 64th hour of life. She

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was hypotonic and icteric. The other system findings were normal. Maternal and infant blood groups were A Rh positive. Laboratory tests showed that total bilirubin level was 25 mg / dl, direct bilirubin level was 0,9 mg / dl, hemoglobin 13,2 gr / dl, reticulocyte count 6,8%, LDH 661 U / L (12-220), direct Coombs test was negative, G6PD U/GR HB was found to be low with 5.5 u / g (10.1-14.9) G6PD U/10x12 RBC 153.7 (290.4-411.6). Exchange transfusion and intermittent phototherapy were performed and the bilirubin level decreased after these interventions. List of medicines and items that the patient should not receive because of G6PD deficiency was given to parents before discharge. At 3 months of age serum level of G6PD was still low.

Case 2

After 2 years, the mother delivered a 3300 g male baby with cesarean at 38 + 5/7 gestational age with 1st minute and 5th minute Apgar score 9, 10 respectively. In the first hour of life she was icteric and total bilirubin level was 8.3 mg/dl was referred to our hospital. Except for jaundice, the other systemic findings were normal. Maternal and infant blood groups were identified as A Rh positive. Serum indirect bilirubin level was 9,4 mg / dl, direct bilirubin level 0,8 mg/dl, hemoglobin 12,5 gr/dl, reticulocyte count 17,9%, LDH 1496 IU/L, direct Coombs test was negative in our hospital. Precursor cells and poikilocytosis were observed in the peripheral smear. G6PD level was normal. The patient's phototherapy limit was 5 mg / dl, and the exchange transfusion limit was 14 mg/dl. Patient received intensive phototherapy. Since laboratory findings implying hemolysis was evident in our patient, minor blood groups were studied from mother and herb baby. Maternal minor blood group results were found to be c (-), C (+), e (+), E (+), Kell (-), Cw (-); and infant's results were c (+), C (+), e (+), E (+), Kell (+), Cw (+). Direct Coombs test, which was found to be negative at the beginning of the treatment was studied with polyspecific technique, we repeated the assay in the light of this minor group incompatibility with dilution technique and detected as (+++) positive. Phototherapy was continued after 2 hours of intensive phototherapy with a total bilirubin level of 11.4 mg/dl and a direct bilirubin level of 0.8 mg/dl. Intravenous immunoglobulin (IVIG) was administered at a dose of 0.5 g/dose for a total of 2 doses for 12 hours. A decrease in bilirubin levels was observed after treatment. The patient was discharged on the 5th postnatal day. We invited the first sbling for minor blood group analysis who was diagnosed as G6PD deficiency two years ago, and found to be anti-c positive. The family was informed about future pregnancies which should be followed for minor blood incompatibility and hemolysis.

DISCUSSION

The most common cause of hemolytic disease of the newborn is blood group incompatibility and occurs as a result of maternal antibodies to antigens on neonatal erythrocytes. Antibodies causing hemolysis of the fetal and neonatal erythrocytes are most commonly seen in ABO and Rh group incompatibility. Minor blood group incompatibility should be considered in cases of hemolytic disease without mostly ABO and Rh incompatibility (1,3). Minor blood group antigens C, c, E, e, Kell, Duffy, Diego, Kidd and MNSs are antigenic systems that cause blood incompatibility between mother and baby (3,4). anti-c antibody is a member of the Rhesus (Rh) family, which is associated with severe fetal and neonatal hemolytic disease. Hemolytic effect is similar to anti-D. Some of the patients with anti-c positivity already have a history of transfusion (3). There was no transfusion history in our cases. Anti-c and anti-Kell are common in the minor blood group incompatibility. Multiple antibodies are present in 8-14% of cases, the most common combination is anti-c and anti-E (5). Our cases had Anti-c positivity in the first and anti-c, Kell and Cw in the second one. Co-existence of anti-c and Kell led to a more severe hemolysis in the 2nd sibling. The second case was treated only with IVIG and phototherapy and didn't require exchange transfusion but jaundice appeared with in the first hour of life. In the first case, blood exchange was performed because of high bilirubin values on 3rd postnatal day. In a study conducted by Markham et al., 1014 pregnant women were evaluated and which 138 were anti-Rh positive, 54 were anti-Rh and other minor blood group antibodies positive, 744 had minor blood group antibodies and 78 had minor blood group combinations (7). In this study, anti-c (+) anti-E (8 cases) and anti-Kell (+) anti-E (5 cases) were found to be the most frequently detected combinations in the absence of anti-Rh. Of 78 patients with multiple minor blood group antibodies, 4 (5.1%) developed hemolytic disease. In the most recent multicenter study in Turkey, 47 of 1624 (2.9 %) hemolytic jaundice developed due to minor group incompatibility (8). Clinically, there is a spectrum ranging from hydrops fetalis and intrauterine lesions to mild jaundice or severe anemia in neonatal period (3). While anti-c is a more serious cause of hemolytic disease, the clinical course of anti-E incompatibility can be very variable (1,7). Some patients with minor blood group incompatibility rarely undergo exchange transfusion. Dajak et al. found severe disease in 14 of 44 hemolytic disease of the newborn due to minor blood group incompatibility and hemolytic disease was more severe in cases with positive anti-c antibody (9). In our series minor blood groups were not studied in the first sibling because of the presence of G6PD and negative Coombs test. G6PD deficiency increases the risk of early-onset neonatal indirect hyperbilirubinemia, which may require phototherapy or exchange transfusion and jaundice may precede anemia. It is an X-linked recessive disorder affecting boys mostly but girls can be also affected. In our country the incidence ranges between 0.5% and 20% (10). In 33% of minor blood group incompatibility Coombs test is positive. The negativity of the direct Coombs test does not rule out incompatibility. This is thought to be due to poor antigenic properties of minor erythrocyte antigens

(1,3). In our case, the direct Coombs test was negative at initialty , but found to be positive (+++) when studied with dilution. IVIG has been used for treatment of alloimmune hemolytic disease. In hemolytic diseases due to minor blood group there were incompatibilities. Even though there is a significant reduction in the need for exchange transfusion, the results of the meta-analysis concerning the feasibility requirement of IVIG-treated infants is still debatable because there is insufficient evidence to conclude that IVIG is beneficial in neonates with hemolytic disease of the newborn and therefore, routine use of IVIG for hemolytic disease newborn is not recommended (11). In our case, IVIG infusion was performed in the early period, and exchange transfusion was not required in the follow-up. It was observed that the findings of hemolysis were relatively stretched. As a result, jaundice in the first 24 hours is pathological jaundice and should be considered first hemolytic diseases. Rh incompatibility and ABO incompatibility are more frequently observed, but minor group incompatibility should always be kept in mind. As in the developed countries, it would be appropriate to establish guidelines for screening all geographies for minor blood groups in our country as well.

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