Case Report

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Hemolytic disease of the fetus and newborn due to minor blood group alloimmunization in a mother of sickle cell disease with multiple alloantibodies

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Abstract:

Hemolytic disease of the fetus and newborn is due to maternal IgG antibodies that transport through the placenta and destroy neonatal red cells. A mismatch of antigens between mother and fetus causes isoimmunization resulting in mild anemia, which may progress to fetal hydrops in the intrauterine period and severe hyperbilirubinemia to kernicterus in neonates. The isoimmunization is mainly caused by Rh-D and ABO antibodies. In this case report, we found neonatal hyperbilirubinemia due to the presence of anti-c alloantibody previously developed in a sickle cell disease (SCD) pregnant female. It is an unusual case of fetal hyperbilirubinemia due to minor blood group alloimmunization in a SCD needing exchange transfusion. Multi-transfused patients should be counseled regarding the need to perform antibody screening frequently before pregnancy for better treatment of both mother and child.

Keywords:

Erythrocyte, hemolysis, IgG antibodies, neonatal hyperbilirubinemia

Introduction

The feto-maternal incompatibility against red blood cell (RBC) antigens results in the alloantibody formation in the mother, and it causes hemolytic disease of the fetus and newborn (HDFN). Most HDFN in a developed country is due to anti-D antibodies.[1] Various reports of anti-c, anti-K, and anti-E alloantibodies causing HDFN were published.[2,3] The Titre and potency of the mother's antibody have a very crucial role for the development of anemia and hyperbilirubinemia in neonates. In sickle cell disease (SCD), alloimmunization is commonly encountered and has been proposed due to chronic inflammatory states along with polymorphism in the TRIM21 gene.[4] Most cases of alloimmunization in SCD disease patients are due to a lack of Rh-Kell matched transfusion, inability to provide leukodepleted red cells, and infrequent antibody screening in pretransfusion testing. Rh-D antibodies are generally seen in alloimmunized SCD patients.[5] These antibodies are of IgG class and may cause HDFN. Hence, SCD patients should have frequently monitored before and throughout pregnancy for better care of both mother and fetus. In this case, the Anti-c and anti-S alloantibody is identified before delivery during pregnancy. Hyperbilirubinemia in a neonate was due to previously formed anti-c of the mother destroying fetal c-antigen-coated red cells.

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Neonate was treated with exchange transfusion, and bilirubin was decreased. We recommend the inclusion of antibody screening on the first antenatal visit, and proper immunohematological workup should be followed throughout pregnancy.

Case Report

A 23-year-old female patient, a known case of SCD, hypothyroid, and chronic hypertensive primigravida at 35 weeks +2 days gestation, was admitted before delivery of the baby. She had received multiple packed red cells (PRCs) transfusion approximately every 3 years. The patient/attendant did not report any history of adverse transfusion reaction to date. At 28 weeks of the current pregnancy, she presented with a vaso-occlusive crisis. The laboratory parameters of this patient were hemoglobin 6 g/dl, and total leukocyte counts 22.39 × 10^3/cumm, platelet count 167 × 103/cumm, lactate dehydrogenase 1419 U/L and sickle hemoglobin 50%, fetal hemoglobin 24.3%. A blood transfusion was requested with the indication of severe anemia. A routine immunohematology (IH) workup as per departmental standard operative procedure revealed a positive antibody screen.

Immunohematology workup of mother at the time of vaso-occlusive crisis

The blood grouping and other IH workup were performed on column agglutination technology (Tulip Diagnostics, Goa, India). The mother blood group is A Rh-D positive. The direct coombs test was negative, but the antibody screen was positive (4+) with screen cells II and III [Figure 1]. Antibody identification was performed using a commercial 16-cell identification panel (Immucor, INC, Norcross, USA) [Figure 2]. The antibody identification panel showed a possibility of multiple alloantibodies. The minor phenotype was performed according to the manufacturer's instructions. The phenotype of the patient was C (+), c (-), E (-), e (+), K (-), Fya (+), Fyb (+), Jka (+), Jkb (-), Lea (-), Leb (-), M (+), N (-), S (-). By selecting cells and considering patient phenotyping, possibilities of Anti-c and anti-S were confirmed. The patient was transfused with two units of Rh, Kell matched and S negative, crossmatch compatible bags. No transfusion reaction was reported. Post transfusion, hemoglobin raised to 8.3 g/dl.

The patient was managed with simple transfusion and other symptomatic therapy. The patient improved clinically and was discharged. The patient was again admitted at 35 weeks gestation for delivery. The preterm neonate born at 35 weeks +2 days was asymptomatic during the initial few hours after delivery, and later, the baby developed severe jaundice. Total serum bilirubin at 23 h of delivery was 20.4 mg/dl. On physical examination, the baby was icteric head to legs, and mild pallor was present. Laboratory findings were as follows: hemoglobin 9.1 g/dl, hematocrit 27.2%, mean corpuscular volume 119.3 fl, platelet count 41 × 103/cumm, white blood cell count 3.78 × 103/cumm, and reticulocyte count 5.7%. Pancytopenia with moderate anisocytosis and many polychromatophilic cells were seen in peripheral blood smear.

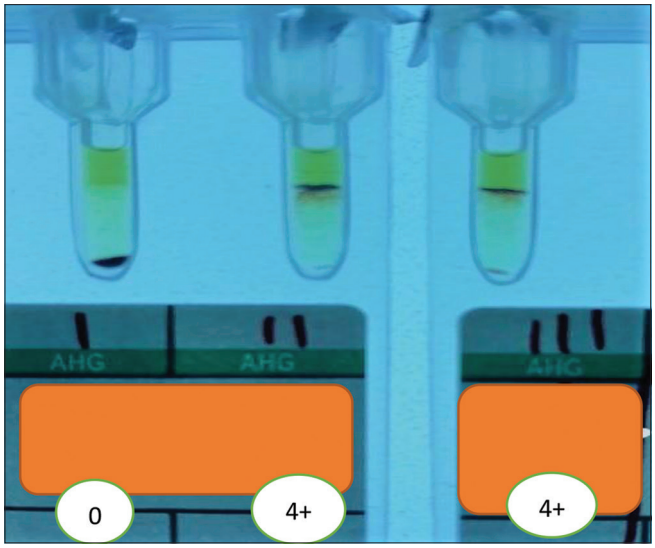

Figure 1: Antibody screening of mother by gel antihuman globulin card

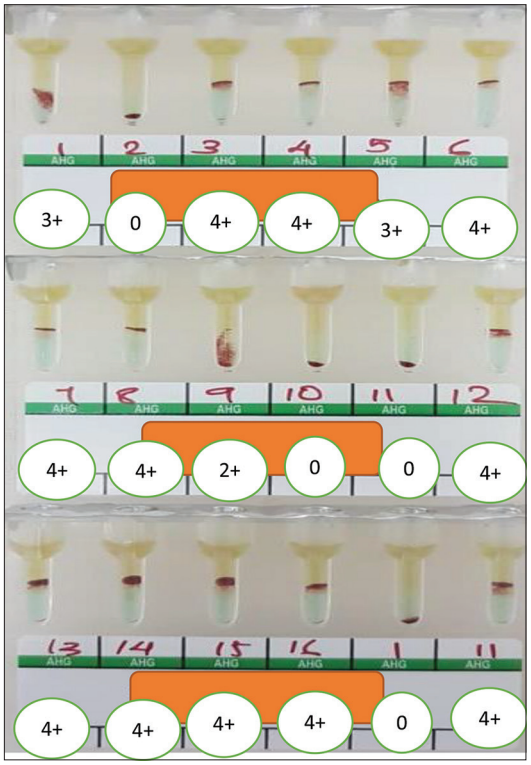

Figure 2: Antibody identification of mother by gel antihuman globulin card

Immunohematology workup of the baby and mother after delivery

Blood grouping is O Rh D positive. Direct coombs test of the baby was positive (4+), with IgG (4+) specificity. Baby's phenotype was C (+), c (+), E (-), e (+), K (-), Le^a (+), Le^b (+), M (+), N (+), S (-). Repeat antibody identification of mother shown the presence of Anti-c, and Anti-S. The titer of anti-c was 256 in the AHG gel card column agglutination method [Figure 3].

Because of the high bilirubin level, the baby was shifted to the neonatal intensive care unit (ICU), and phototherapy was started. Serial monitoring of total bilirubin showed a raising trend and at 23 h' bilirubin was 20.3 mg/dl, and an exchange transfusion was planned. The O Rh-D Positive (c and S phenotype negative), leukoreduced PRCs within 7 days' storage, was crossmatched compatible with both mother and baby. Reconstituted PRCs with AB-positive plasma and final hematocrit of 55% were issued. Two-stage exchange transfusion and intensive phototherapy significantly lowered the total bilirubin level to 7.4 mg/dl. The baby was discharged from the neonatal ICU on day 2.

Discussion

Neonatal hyperbilirubinemia can be due to immunological and nonimmunological causes. ABO and Rh-D incompatibilities are the most common immunological cause.[6] About 3%–5% of neonatal hemolytic jaundice is due to minor antigens incompatibility.[7] Maternal IgG alloantibodies crossed the placenta and bind with specific paternally inherited fetal RBC antigens. This causes intravascular or extravascular hemolysis resulting in severe anemia and hyperbilirubinemia of the fetus. Increased level of neurotoxic indirect bilirubin will cross the blood–brain barrier and results in acute to chronic neurological manifestations such as choreoathetosis, gaze abnormality, and sensorineural hearing loss.

Figure 3: Antibody titer of mother by gel card method

Antibodies against Rh, Kell, Duffy, Kidd, MNS, and Diego antigens are the most common causes of HDFN.[8] Several reports of hemolytic disease were available from Korea, China, and Taiwan, which were caused by anti-C, anti-E, anti-M, anti-Jk, and anti-Mi.[9]

Alloimmunization in the mother can be due to previous exposure to transfusion, pregnancy, or abortion. IgM antibodies are initially produced after exposure of antigens and then a gradual transition occurs for the formation of IgG antibodies. Anti-Rh antibodies are primarily IgG type and Cross placenta.

Direct Coomb test is positive due to IgG antibodies coating well-developed fetal Rh antigens.[10] As Rh antibodies are noncomplement activating, RBC destruction occurs primarily extravascular, causing severe anemia and hyperbilirubinemia. Rh antibodies often persist in circulation for years. Delayed type hemolytic reactions are developed mostly in SCD, due to an anamnestic response of low titer antibodies. These antibodies were often persisting in circulations for many years.[11]

History of multiple transfusions, crises, and hidden antepartum hemorrhage could be the reason for the alloimmunization of the mother. Both anti-c and anti-S are of IgG type, and they can easily cross the placenta. Baby's inherited phenotype is c (+) and S (-). Since the mother had a high titer for anti-c antibodies, baby had clinically significant jaundice and features of hemolysis requiring phototherapy and exchange transfusion. Antibody identification from eluted newborn RBCs was not made due to insufficient red cells. The strong DCT-positive baby, presence of c-antigen on newborn RBC, and high titer of anti-c IgG antibody of the mother was strongly suspected cause of neonate hyperbilirubinemia in our case. The antibody screen should be performed before the next transfusion and in the forthcoming pregnancy. Further, c and S antigen-negative PRCs should be given to the mother for future transfusion purposes.

Conclusion

In cases of neonatal hyperbilirubinemia in which a mother has a history of transfusions, especially SCD, pregnancy, and abortion, screening of alloantibodies

should be considered. If alloantibodies are detected, antibody titer of the mother should be performed regularly as per the institute's protocol. Postdelivery fetal monitoring, including DCT, hemoglobin should be performed routinely for neonates of the mother with a history of multiple alloantibody. Proper documentation of prior workups should be done, and reports should be handed over to the patient. Counseling regarding the awareness of alloimmunization, fetal complications, the requirement of exchange transfusion should be discussed with the clinician and patient.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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