Case Report

Hemolytic disease of the fetus and newborn caused by anti-E

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Abstract:

Objective: Maternal allo-antibody production is stimulated when fetal red blood cells are positive for an antigen absent on the mother's red cells. The maternal IgG antibodies produced will pass through the placenta and attack fetal red cells carrying the corresponding antigen. Allo-immune hemolytic disease of the fetus and newborn caused by anti-E rarely occurs. **Case summary:** We report two cases of anti-E hemolytic diseases in neonates. One of the neonates had severe hemolysis presenting with severe anemia, thrombocytopenia, and conjugated hyperbilirubinemia, while the other had moderate anemia and unconjugated hyperbilrubinemia. Although both the neonates were treated by phototherapy and intravenous immunoglobulin, one of them received double volume exchange transfusion. **Conclusion:** There appeared to be an increase in the occurrence of hemolytic disease of the fetus and newborn caused by Rh antibodies other than anti-D. In this case report, both patients presented with anemia and hyperbilirubinemia but were successfully treated, with a favorable outcome.

Key words:

Allo-antibody, anti-E, hemolytic disease of the fetus and newborn

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Introduction

Maternal red cell allo-immunization occurs when the fetus is positive for an antigen that is absent on maternal red cells. The mother is stimulated to produce immunoglobulin G (IgG) antibodies against the positive fetal red cells which pass through the placenta and destroy the antigen-positive fetal red cells. Clinically significant allo-antibodies other than anti-D such as anti-E, anti-K, and anti-c occur in 1:300 pregnancies and risk of hemolytic disease of the fetus and newborn (HDFN) caused by these antibodies is 1:500.[1] Anti-E is the most common clinically significant allo-antibody detected in the Malaysian population.[2] We report here two cases of anti-E HDFN in two Malay infants.

Case Reports

Case 1

A full-term male neonate born to a 32-year-old G2P2 Malay lady was noticed to have jaundice on day 1 after birth. His birth weight was 2.96 kg. The mother and the baby were grouped AB and B, respectively, both being positive for RhD antigen. The baby was shifted to neonatal intensive care unit (NICU) on the following day with hepatomegaly 3 cm and splenomegaly 5 cm below the costal margin. Direct antiglobulin test (DAT) on the neonate's red cells was strongly positive (4+). Hemoglobin was 6.2 g/dL. A sudden rise of total serum bilirubin (TSB) level from 102 μmol/L on day 1 to 401 μmol/L within 24 h prompted to double volume exchange transfusion (ET). The hyperbilirubinemia was mainly of conjugated bilirubin 1 day post-ET [Figure 1].

Investigations for infectious causes such as blood culture, urine microscopy, and culture were negative. Liver enzymes such as alkaline phosphatase, alanine transaminase, and aspartate amino transferase were also within the normal ranges. G6PD screening was negative. No evidence of biliary atresia was found. Anti-E was detected and identified in the mother's serum and eluate from the baby's red cells. Rh genotype was performed for the mother, father, and the neonate. The mother was typed as *R1R1* (*DCe/DCe*), father *R1R2* (*DCe/DcE*). Although the baby's red cells reacted with all the Rh subtype reagents there by typing as *R1R2* (*DCe/DcE*), the results could not be validated as the auto-control test was positive as well. The neonate was placed on single phototherapy and was given intravenous immunoglobulin (IVIG) at a dose of 0.5 g/kg over 4 h.

The peripheral blood film of the neonate showed evidence of hemolysis such as polychromasia, nucleated red blood cells (NRBCs), and red cell fragments. The baby also presented with thrombocytopenia that was not associated with any known infection. We presumed this could be allo-immune in nature, though no attempt to test for platelet-specific antibodies was made due to lack of facility. He was clinically fit at day 8 of life with slightly lower total serum bilirubin of 230 μmol/L at the time of discharge. The baby was discharged on day 8 of life hale and hearty.

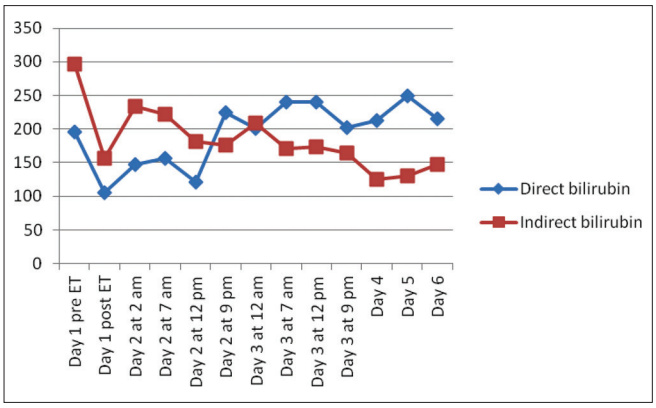

Figure 1: Concentration of direct and indirect bilirubin (μmol/L) in the infant's serum from the time of admission to day 6

Case 2

A male neonate was delivered via spontaneous vaginal delivery (SVD) at 30 weeks of gestation by a 33 year-old Malay lady G7P7. The mother had a history of premature deliveries in all but one of her previous pregnancies. Her blood group was O RhD positive and was Rh-subtyped as *R1R1* (*DCe/DCe*). Post-SVD antibody screen test in her serum was positive with antibodies identified as anti-c and anti-E. The neonate's birth weight was 1.8 kg. He was transferred to NICU. He was noticed to have jaundice (serum bilirubin 138 μmol/L) at 14 h after birth. His blood group was B RhD positive with Rh-subtype *R1R2* (*DCe/DcE*). DAT was positive (2+). As in the first case, the Rh-subtype results may be interpreted with caution in light of the DAT being positive. A possibility of the ABO HDFN was opened but was ruled out with an extent that the eluate preparation from the baby's red cells showed anti-E only (not anti-c). The neonate became moderately anemic on day 5, with a hemoglobin level of 10.2 g/dL. No evidence of hemolysis was seen on the blood film. The patient was managed with phototherapy, IVIG, and transfusion of 30 cc of red cell concentrate. In light of underlying coagulopathy noticed at 6 h of life (with activated partial thromboplastin time 93.70 s, prothrombin time 20.8 s, and INR 1.80), a dose of 20 cc of fresh frozen plasma was also administered. He was discharged on day 14 of life as requested by the parents. His follow-up visit showed normal developmental milestones with consistent increase in body weight.

Discussion

With the introduction of anti-D prophylaxis, the incidence of Rh HDFN has been reduced. ABO foeto-maternal blood group incompatibility is the main cause of HDFN.[3] Other red cell allo-antibodies such as anti-c, anti-C, anti-E, and anti-e of the Rh blood group system and anti-K of the Kell blood group system have been reported occasionally as rare causes of HDFN.[4,5] Previous study[6] reported that most cases of HDFN caused by Rh antibodies other than anti-D have been detected in RhD-positive women. The two cases we report here were also in RhD-positive women. Here we described two cases of HDFN due to anti-E. Both the babies showed a positive DAT and corroborating findings of anti-E being present in serum samples of the respective mothers. Eluates obtained from the babies' red cells showed anti-E antibody specificity thus providing evidence for a cause of HDFN in both cases. In case 1, there is evidence of hemolysis seen on blood picture (anemia, polychromasia, NRBCs), whereas in the second case no evidence of hemolysis was seen on blood picture. The Rh genotypes in both cases were supportive of the hypothesis on anti-E as the cause of HDFN.

It has been reported previously that the risk of allo-antibody production is unknown during pregnancy, but foeto-maternal hemorrhage at the time of delivery is a frequent stimulus.[7] Both mothers in the present report were probably sensitized during previous pregnancies. Presentations of case 1 (anemia, conjugated hyperbilirubinemia, thrombocytopenia) are consistent with two earlier reported cases of HDFN caused by Rh antibodies other than anti-D.[8,9]

Conclusion

This case report shows that HDFN caused by anti-E may be moderate or severe in its presentation and brings to attention the necessity of introducing antibody screening for pregnant women as part of the antenatal care to look for significant allo-antibodies other than anti-D. Those mothers found to be allo-immunized should be monitored closely for measurement of maternal antibody titer and, in more severe conditions, for amniotic fluid analysis to monitor the fetus.

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