Case Report:
Severe Hemolytic Disease of the Newborn in a Group B African-American Infant Delivered by a Group O Mother

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Abstract. Maternal-fetal ABO incompatibility is a common hematological problem affecting the newborn. In general, hemolysis is minimal and the clinical course is relatively benign, rarely causing the escalating levels of hyperbilirubinemia and significant anemia commonly associated with Rh hemolytic disease of the newborn (HDN). The incidence of HDN ranges from one in 150 births to 1:3000 births, depending on the degree of anemia and level of serum bilirubin. The etiology of ABO hemolytic disease of the newborn (ABO-HDN) is complex because anti-A and anti-B antibodies are composed mainly of IgM. Since only IgG antibodies cross the placenta, those pregnant women with high levels of IgG anti-A, B, anti-A, or anti-B with an ABO incompatible fetus will be the ones to give birth to an infant with ABO-HDN. We describe a case of a B/Rh positive term newborn born to an O/Rh negative African-American mother demonstrating aggressive hemolysis and a robust response of the bone marrow. This case was successfully managed with phototherapy and simple RBC transfusion without the need for exchange transfusion.

Keywords: hemolytic disease of the newborn, neonatal blood exchange, hemolysis, hyperbilirubinemia

Introduction

Hemolytic disease of the newborn (HDN) is a clinical condition in which fetal red cells are destroyed by maternal IgG alloantibodies directed against paternal antigens. D positive pregnancies in women previously immunized to the D antigen may result in severe HDN. In contrast, maternal-fetal ABO incompatibility (eg, O mother and A child) typically results in mild HDN [1]. The consequence of severe red cell alloimmunization is often fetal death or very premature delivery. In moderately affected cases, the fetus does not develop significant anemia during pregnancy but may do so upon delivery. In mild cases of RBC alloimmunization, there can be a moderate rise in unconjugated bilirubin. Before the practice of giving prophylactic anti-D to prevent the sensitization of Rh-negative pregnant women, Rh-associated HDN and hydrops fetalis were relatively common. The incidence of HDN ranges from one in 150 to 1:3000 births depending on the degree of anemia and level of bilirubin [2]. In the USA, 6.9% of all births are of infants with maternal-fetal ABO incompatibility and ABO-HDN is now the single most common cause of neonatal jaundice [3]. The hemolysis is widely accepted to follow a relatively benign course, rarely causing hydrops fetalis. Case reports of fetal hydrops secondary to ABO incompatibility are particularly rare, with only 9 cases reported to date [4-8]. We describe here the case of a full term, African-American neonate whose red cells typed B, born to O mother, who demonstrated aggressive hemolysis and anemia within hours of delivery, and who then showed a compensatory robust hematological response.
Case Report

A term, African-American female neonate, born to a 21-yr-old woman G2P1001, was found to have jaundice at 4 hr after birth. The neonate's red cells typed B, D positive, while the mother's red cells typed O, D negative. The mother’s anti-B antibody titer was 256. A screen for fetomaternal hemorrhage was negative. The direct antiglobulin test (DAT) was positive with the cord red cells, and anti-B, but not anti-A, antibody was detected in the neonatal red cell eluate. The infant’s blood hemoglobin and serum total bilirubin (TB) concentrations were 10.6 g/dl and 9.6 mg/dl, respectively. Her erythrocyte glucose-6-phosphate dehydrogenase (G6PD) activity was normal and a sickle cell test yielded negative results.

As shown in Fig. 1, the peripheral blood smear demonstrated numerous nucleated RBCs, spherocytes, prominent spherocytes, polychromasia, and mitotic figures. An infectious disease evaluation was negative. The patient was diagnosed as hemolytic disease of the newborn due to ABO incompatibility (ABO-HDN). The infant’s TB peaked at 16.1 mg/dl on day three (Fig. 2), which prompted 2 sessions of phototherapy and the transfusion of 30 ml of red blood cells. Exchange transfusion was not required. The infant was discharged on day 8 with a TB of 3.9 mg/dl.

Discussion

In HDN, fetal RBCs are destroyed by maternal alloantibodies directed against paternal antigens. This case of ABO-HDN is unusual in its severity, peripheral blood smear abnormalities, and degree of hyperbilirubinemia. The evidence supporting ABO incompatibility as the cause of the severe hemolytic anemia in this patient consists of maternal IgG anti-B antibodies found in the neonatal eluate. The neonatal blood smear showed changes typical of hemolysis (Fig.1). Inherited causes, such as G6PD deficiency and sickle cell disease, were excluded. Congenital infection screening tests were negative. No other causes of transient or severe hemolysis could be identified.

ABO-HDN is a common condition occurring in about 15% of infants with A or B blood types born to blood type O mothers and, unlike non-HDN-ABO incompatibility, is usually a problem of the neonate rather than of the fetus [1]. Hydrops fetalis in association with ABO incompatibility is
extremely rare [4-8], mainly because anti-ABO antibodies are typically IgM and do not cross the placenta. Additionally, when IgG anti-A,B, -A, or -B antibodies are produced, ABO antigens on fetal tissues act as a sink for circulating maternal antibodies. Finally, A and B antigens are only weakly expressed on neonatal RBCs. ABO-HDN is therefore usually mild and characterized by a negative or weakly positive DAT. ABO-HDN rarely requires red cell exchange transfusion, in contrast to HDN due to anti-D or other antibodies.

Several studies have established that ABO hemolytic disease is more common in blacks (South African and African-American) and in children of mixed racial origin than among white infants and other races [9-10]. In published cases, most affected neonates also belonged to the B blood group [4-6,9]. Adewuyi et al [11] found that serum hemolytic activity of anti-A and anti-B antibodies from black subjects was higher than the corresponding activity found in white subjects. Their study showed that the hemolytic activity of anti-B antibodies is higher than of anti-A antibodies within each racial group.

Ziprin et al [9] in an analysis of their 2 cases of ABO-HDN and 6 other cases in the literature, made the observation that severe hemolysis usually involves both the anti-B antibody as well as black mothers. Another study confirmed the increased incidence of ABO-HDN in black infants with blood type B, but showed no increase in the severity of the disease [10]. The increased incidence of ABO-HDN in black and blood group B infants is believed to result from environmental factors rather than genetic factors [12]. Interestingly, the severe hemolysis seen in the present case also involves both the black ethnic background and the presence of anti-B maternal antibodies.

This case demonstrates that ABO incompatibility is not always a benign condition and that HDN may be of sufficient severity to require management of infants born to group O mothers. Also, this case highlights the fact that red cell exchange is not necessarily needed for ABO-HDN, even with significant hemolysis and a prominent bone marrow response. Phototherapy may be sufficient, with or without red cell transfusion.

References