Case Report:
Severe Hemolytic Disease of the Newborn Due to anti-Di\textsubscript{b}
Treated with Phototherapy and Intravenous Immunoglobulin

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Abstract. The Di\textsubscript{b} antigen usually occurs with high incidence, except in certain Asian and South American Indian populations. In general, hemolysis caused by anti-Di\textsubscript{b} is not severe and its clinical course is benign. We report a Korean neonate with severe hemolytic disease of the newborn caused by anti-Di\textsubscript{b}. The phenotype and genotype of the Diego blood group system of the patient and his mother were Di(a+b+) and Di(a+b-), respectively. The mother’s serum and eluate from the neonate’s erythrocytes contained anti-Di\textsubscript{b}. This case was successfully managed with phototherapy and high dose iv immunoglobulin. Since most commercial antibody detection panels do not contain Di(b-) red cells, it is important to consider anti-Di\textsubscript{b} in cases of hemolytic disease of the newborn caused by an antibody against a high frequency antigen.

Keywords: anti-Di\textsubscript{b}, hemolytic disease of the newborn, Diego blood group, phototherapy, iv IgG

Introduction

The Diego blood group mainly consists of 2 independent pairs of antigens, called Di\textsuperscript{a}/Di\textsubscript{b} and Wr\textsuperscript{a}/Wr\textsuperscript{b} [1]. Both pairs of antithetical high and low incidence antigens are carried on band 3 proteins, and a single amino acid substitution (Pro for Leu) determines Di\textsubscript{b} rather than Di\textsuperscript{a} [2]. The Di\textsuperscript{a} antigen is rare in Caucasian persons, but is mostly found in Asian populations, including Chinese, Korean, and Japanese (5-8%), and in South American Indians (7-54%) [3-4]. Blood donors with Di(b-) phenotype are almost exclusively found in the Asian and Indian populations [3]. There have been about 30 reported cases of hemolytic disease of the newborn (HDN) due to anti-Di\textsubscript{b}, mostly in Japanese [3]; 2 additional cases in Koreans have been reported in the Korean literature [5,6]. We report a baby born to a Di(b-) Korean mother who demonstrated severe hemolysis and hyperbilirubinemia due to anti-Di\textsubscript{b}. The baby was successfully treated with phototherapy and high-dose iv immunoglobulin (iv IgG).

Case Report

A term, male neonate was born to a 32-yr-old Korean woman who had a history of an early abortion and who had received a red cell transfusion during a surgical operation 13 yr previously. At 24 hr after delivery, the baby was found to have jaundice with a serum total bilirubin (TB) level of 14.9 mg/dl and blood hemoglobin (Hb) level of 12.8 g/dl. On day 3 of life, the Hb was 8.0 g/dl, the TB was 16.1 mg/dl, and the peripheral blood smear demonstrated schistocytes, polychromasia, and numerous nucleated RBCs. Spherocytes were not

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found. The neonate’s and the mother’s red cells typed B, Rh⁺, and AB, Rh⁺, respectively. The neonate’s red cells reacted positively (3+) in the direct antiglobulin test (DAT) and the serum reacted positively (2+) in the indirect antiglobulin test (IAT) using IgG-specific Coombs serum. The serum and eluate from the red cells were reactive at high titer (1:1024) with the entire panel of red cells that was tested (DiaMed, Cressier, Switzerland).

The mother’s serum had a positive IAT (3+) and her red blood cells tested negative with the DAT. Her serum also reacted with the entire panel of red cells, using both the gel agglutination method (LISS and enzyme) and the standard tube (LISS) techniques. The mother had not been screened for irregular antibodies during pregnancy.

Because of the suspicion of HDN due to an antibody against a high frequency red cell antigen, the mother’s red cells were extensively phenotyped. Her phenotype was found to be: CcDEe, K-k+, Kp(b+), Js(b+), Jk(a+b-), Fy(a+b-), M+N-S-s+, and Di(a+b-). The Diego phenotyping was performed using a commercial polyclonal Di⁻ antibody (DiaMed) and a monoclonal anti-Di⁻ antibody from the Japanese Red Cross Blood Center (Osaka, Japan).

The Diego phenotype was confirmed by genotyping for Di⁻ and Di⁻ by the PCR-SSP method of Wu et al [7]. A study of the maternal family showed the mother and one of her brothers to be Di(a+b-), while her parents, a sister, and the baby were all Di(a+b+). The antibody present in the mother’s serum did not react with her brother’s red cells, thus confirming the specificity of the antibody responsible for HDN as anti-Di⁻.

The baby was not able to undergo exchange transfusion because the diagnosis was delayed, but the baby was started on a course of phototherapy on the 2nd day of life. Despite this treatment, the serum total bilirubin level increased to 16.1 mg/dl. Intravenous IgG (500 mg/kg) was administered over 4 hr. On the day following iv IgG, the serum TB level fell to 11.9 mg/dl. The condition of the baby stabilized and he was discharged from the hospital 9 days after birth with a serum TB level of 7.4 mg/dl and a blood hemoglobin level of 9.4 g/dl. At 6 months of age, a DAT performed on the baby’s red cells was negative.

Discussion

Blood donors with the Di⁻ phenotype are included in the rare blood donor category by the ISBT Working Group on Rare Blood Donors [8]. The frequencies of the Diego blood group phenotype in Koreans are 0.25% for Di(a+b-), 9.75% for Di (a+b+), and 90% for Di(a-b+) [5]. The gene frequencies for Di⁻ and Di⁻ in Koreans are 0.051 and 0.949. Anti-Di⁻ is usually formed during a previous mismatched pregnancy or following a transfusion [3]. In our case, it is likely that the mother had anti-Di⁻ from a previous transfusion.

While HDN caused by anti-Di⁻ has been considered to be associated with only mild hemolysis and only rarely to cause hydrops fetalis [9], it has also been associated with severe jaundice [10-11]. Two previous cases that were reported in Korean babies were severe and required exchange transfusion with Di⁻ negative red cells from maternal relatives [5,6]. A previous report cited an association of maternal antibody titer and severity of disease [3]. In our case the maternal titer was 1:1024, and the baby required treatment.

While exchange transfusion with antigen negative cells would be standard treatment for severe HDN, iv administration of IgG has been reported to slow hemolysis of antibody-coated red cells [12]. A systematic review of the literature indicated that iv IgG is effective in reducing the exchange transfusion rate in neonates with HDN [13]. Therefore, such therapy appears to be therapeutically effective in HDN cases, when it is impossible to obtain antigen-negative red cells.

Since Di⁻ antigen is a high incidence antigen, most commercial antibody identification panels do not include Di⁻ red cells. Moreover, the limited access to specific antisera to this antigen makes it difficult to identify Di⁻ donors. Genotyping techniques make it possible to identify donors for exchange transfusion. It is important to consider anti-Di⁻ in cases of HDN due to antibody against a high incidence antigen. Reference laboratories should be used to identify appropriate donors if antigen-negative family members cannot be found. In our patient, in whom exchange transfusion was not performed, we found that iv IgG was therapeutically effective.
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References


