Introduction

The HDFN can lead to fetal hemolytic anemia, jaundice, premature birth and is an important cause of neonatal morbidity and death [1,2]. Most cases of HDFN, caused by naturally formed ABO antibodies, generally lead to minimal or mild symptoms. Although the incidence of anti-D associated HDFN has drastically reduced with Rh immune globulin prophylaxis, HDFN due to other maternal red cell alloantibodies still remains a concern [3].

The MNS is a highly complex blood group system consisting of 49 antigens. S (MNS3) and s (MNS4) are a pair of antithetical antigens pair of this system. Red cells of about 1% African Americans and a higher incidence of black Africans are S-s- and lack the high frequency antigen U (MNS5). If immunized, these individuals may produce anti-U [4]. The HDFN owing to anti-U has rarely been reported. In this case, a rare red blood cell alloantibody could cause hemolytic transfusion reaction and hemolytic disease in the fetus and newborn [5,6]. Here, we describe the case of a female newborn presenting a strongly positive direct antiglobulin test due to an anti-U.

Case report

A female newborn delivered at 39 weeks’ gestation in Herculano Pinheiro Maternity Hospital, Rio de Janeiro, Brazil, weighing 3.858 g, Apgar score 9/9, jaundiced 1+/4+, swollen eyelids, with eyelid edema, presented a strongly positive Direct Antiglobulin Test (DAT) with evidence of clinically significant mild hemolysis. She received double phototherapy on her first day of life and her bilirubin level was 20.0 mg/dL within 48 hours after birth. Due to the presence of maternal alloantibodies in the blood of the newborn against the high frequency antigen, and the consequent difficulty in performing immediate diagnosis and providing opportunities for the
The maternal red blood cell MNS phenotyping showed a very rare pattern (M,N,S,u). The erythrocytes of the newborn were phenotyped as O ccDee, KEL (-1,2), FY(1,2), JK(1,2), MNS(1,-2, 3, 4) and LU(-1,2). Anti-U was recovered from cord blood using acid eluate technique. The gel method was used to determine blood group systems (Biorad®, Brazil), detecting and identifying irregular antibodies, direct antiglobulin, and crossmatching. A sample of maternal blood was sent for further diagnostic clarification to the Transfusion Agency of the Evandro Chagas National Institute of Infectious Diseases and, from this, to the Immuno–Hematology Laboratory of Bio–Rad. The mother’s phenotypic (Figure 1) profile was determined to be group O, ccDee, KEL (-1,2), FY(-1,2), JK(1,2), MNS(1,2,3,4,5) and LU(-1,2); and her serum contained anti-U. The mother’s serum was tested against four U– erythrocytes, showing no reactivity confirming the presence of anti–U alloantibodies. Additionally, the selective adsorption procedure with homologous red blood cells was performed to adjust for the presence of possible other alloantibodies. After the adsorption of anti–U, the presence of concomitant attacks was not observed.

In the newborn, the decrease in total bilirubin levels was 13.0 mg/dL allowing that quadruple phototherapy was evolved into double phototherapy after 48 hours. After 24 hours of double phototherapy, new laboratory results showed total bilirubin 12.1 mg/dL, direct bilirubin 0.9 mg/dL, Hemoglobin 12.0 g/dL and hematocrit was 36.5%. Simple phototherapy was established for 24 hours, at the end of which the newborn exams maintained total bilirubin 12.1 mg/dL, direct bilirubin 0.9 mg/dL and jaundice 1+/4+. The newborn was discharged from the maternity ward at 9 days of age, sustaining jaundice 1+/4+, hematocrit 24.8% and hemoglobin 8.6 g/dL. She presented good general and hemodynamic conditions, and was directed to a follow–up clinic of Perinatal Hemolytic Disease at the Martagão Gesteira Institute of Childcare and Pediatrics. On admission to this clinic at 11 days of life, she presented signs of hemodinamically worsening, positive direct antiglobulin (IgG/4+), hematocrit 22.0%, hemoglobin 6.5 g/dL, when she underwent a transfusion procedure with packed red blood cells 10 mL/ kg, respecting the maternal phenotype for ABO, Rh, Kell, Kidd and Duffy systems. In close follow–up at the institution, the initiation of therapy with ferrous folic acid and sulfate was instituted to a lesser extent, with a progressive improvement in hemimetric levels and a decrease in Direct Coombs. At 2 months and 6 days of age, she received discharge from the clinic, with negative DAT, Hematocrit 31.5% and Hemoglobin 10.5g/dL.

**Discussion**

The severity of HDN varies from asymptomatic to fatal. The S–s– phenotype is typically found in people of African origin and represents a challenge in transfusion sets, especially when S–s– patients develop anti–U [7]. In addition to the anti–U alloantibody, the maternal phenotype Fy(a–b–) could also suggest the presence of another rare antibody against high frequency antigen: anti–Fy1. However, in the case of Brazilian African–descent women, the phenotype Fy(a–b–) is the product of a point mutation in the GATA promoter region of the Duffy gene, being responsible for the absence of antigen expression in red blood cells but not in other tissues. This frequency ranges from 60% to 100% in the black population.

Despite of the fact that anti–D alloantibodies are the most common cause of newborn hemolytic disease, antibodies against other blood group antigens could cause serious and even fatal fetal and perinatal hemolytic diseases. A literature review suggests that the pathophysiology of anti–U manifestation is similar to Rh isoimmunization. The anti–U antibody can develop because of pregnancy or blood transfusion in 1.2% of African descent susceptible to developing the antibody (U–). Finally, is necessary to point out that when an antibody against a high frequency erythrocyte antigen is identified in African or American–descent pregnant women, anti–U should be considered and the fetus or newborn should be monitored/ followed up until the safe finding of complete consumption of the maternal alloantibody.

**References**

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