


Case Report

A Rare Disease in Newborns; Anti-E Subgroup Incompatibility, Case Report

Yenidoğanda Nadir Görülen Bir Hastalık ; Anti-E Subgrup Uyuşmazlığı, Olgu Sunumu

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ABSTRACT

Hemolytic disease of the newborn is caused by maternal erythrocyte antibodies reacting to fetal erythrocytes. While it is commonly associated with Rh and ABO incompatibilities, the incidence has decreased with the use of anti-D immunoglobulin, resulting in a rise in subgroup incompatibilities. Subgroup incompatibility accounts for 3-5% of neonatal hemolytic diseases, ranging from indirect hyperbilirubinemia to exchange transfusion in severity. The patient in this study was observed to be pale during the first newborn examination and had anemia in the cord blood gas analysis. As a result of detailed examinations, the patient was diagnosed with anti-E subgroup incompatibility. This case report presents a newborn diagnosed with anti-E subgroup incompatibility who received intravenous immunoglobulin treatment, erythrocyte transfusion and intensive phototherapy, requiring additional erythrocyte transfusion at the 1st-month follow-up.

Keywords: subgroup incompatibility, newborn, jaundice, phototherapy

ÖZET

Yenidoğanın hemolitik hastalığı, maternal eritrosit antikorlarının fetal eritrositlere yanıtıyla oluşur. Çoğunlukla Rh ve ABO uyumsuzluklarında görülmesine rağmen anti-D immunglobulin uygulaması sonrasında sıklığı azalmıştır. Göreceli olarak subgrup uyumsuzluklarıyla karşılaşma ihtimalimiz bu nedenle artmaktadır. Subgrup uyumsuzluğu, yenidoğan hemolitik hastalıklarında %3-5 oranında karşımıza çıkmaktadır. Subgrup uyumsuzluklarında indirekt hiperbilirubinemiden kan değişimine varan spektrumda olgu karşımıza çıkabilmektedir. Çalışmadaki olgunun yenidoğan ilk muayenesinde soluk olduğu izlenmiş ve kord kan gazında anemisi olduğu tespit edilmiştir. Detaylı tetkikleri sonucunda Anti-E subgrup uyumsuzluğu tanısı almıştır. Bu yazıda IVIG tedavisi, eritrosit transfüzyonu, yoğun fototerapi aldıktan sonra tedavisi tamamlanarak taburcu edilen, taburculuk sonrası 1. ay kontrolünde tekrar eritrosit transfüzyonu yapılması gereken bir yenidoğan olgusu sunulmuştur.

Keywords: alt grup uyumsuzluğu, yenidoğan, sarılık, fototerapi

INTRODUCTION

Neonatal jaundice is one of the common diseases of the newborn. The most common cause is hemolytic diseases arising from blood incompatibilities. Currently, due to the widespread use of anti-D gammaglobulin, the frequency of Rh incompatibility has decreased

and the incidence of subgroup incompatibility has increased. (1-5) D, C, c, E antigens in the Rhesus (Rh) system and K antigens in the Kell system are the most common subgroup antigens. (6-8) Subgroup incompatibility occurs in 3-5% of neonatal hemolytic diseases.

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The clinical presentation may appear in a vast spectrum in patients with subgroup incompatibility. Patients may be asymptomatic or may present with severe hyperbilirubinemia and hemolysis findings that require exchange transfusion. (1,3,5–7) Here, a case of neonatal hemolytic disease due to anti-E is presented because of the rarity of such cases.

CASE REPORT

A 2230-gram patient born to a 33-year-old mother with AB Rh (+) blood group, in her 3rd pregnancy, one miscarriage, 2nd living, 38-week mature meconium-stained intrauterine growth retardation (IUGR), was observed to be pale on first examination. Systemic examination was normal. The patient's hemodynamics were stable. Cord blood gas analysis revealed that the patient's hemoglobin (Hb) value was 7,3 g/dl. A complete blood count test was performed at the second postnatal hour. The patient's Hb value was 7,7 g/dl, platelet value was 117.000/uL, blood group was 0 Rh (+), and direct Coombs value was 4 positive. The patient had bloody stools twice in the first 24 hours of the postnatal period. In the complete blood count taken for control purposes at the sixth postnatal hour, the Hb value of 5,5 g/dl and platelet value were 100,000/uL. 15 ml/kg erythrocyte suspension was administered as a single dose. It was observed that the Hb value increased to 12 g/dl.

In the patient's biochemistry tests taken at the 6th hour, the total bilirubin value was 7,84 mg/dl, the direct bilirubin value was 1,19 mg/dl, and the LDH level was 755 U/l. The reticulocyte value was 7%. Phototherapy was started according to Bhutani's jaundice curves. (9) The patient was administered intravenous immunoglobulin (IVIG) (1 g/kg/dose) treatment at the sixth postnatal hour due to the rapid increase in bilirubin levels. IVIG treatment was applied once and over two hours. Phototherapy was terminated when the patient's total bilirubin level decreased to 3 mg/dl at the 48th hour. Rebound hyperbilirubinemia did not develop.

Reticulocyte value increased by 24,1%. TORCH tests were negative. There were signs of hemolysis (anisocytosis, polychromasia, tear drop cells, stomatocytes) in the patient's peripheral blood smear. Transfontanel ultrasound performed when the patient was 2 days old was normal. Abdominal ultrasound of the patient revealed mild hepatosplenomegaly. The subgroup analysis of the patient resulted in C (+), c (+), E (+), e (+), and Kell (-). Hb electrophoresis resulted in HbA 82,5%,

HbA2 3,44%, and HbF 14%. Haptoglobin level was low. (<8 mg/dl)

The mother's indirect Coombs test was positive. Blood tests revealed that mild thrombocytopenia developed after the abortion. Subgroup analysis of the mother resulted in C (+), c (+), E (-), e (+), Kell (-). When the subgroup analyses were compared, it was determined that the patient had anti-E subgroup incompatibility.

When the patient's Hb level decreased to 9,6 g/dl at the 24th hour, a subgroup-appropriate 15 ml/kg erythrocyte suspension (E negative) was administered for the second time. During the patient's follow-up, it was observed that there was no decrease in hemoglobin value. Platelet values ranged between 64.000 and 117.000/uL. The patient's thrombocytopenia could be due to IUGR. The persistence of thrombocytopenia during hospitalization was evaluated as iatrogenic due to multiple blood tests.

The patient, whose general condition was stable, was discharged at the age of 5 days and taken to the outpatient clinic. The patient was referred to the Pediatric Hematology Department for follow-up and treatment. During the patient's follow-up in the Pediatric Hematology Clinic, a complete blood count check was taken at the age of 28 days. The patient underwent an erythrocyte transfusion because the Hb value was 6.1 g/dl. In subsequent follow-ups, the patient's hemoglobin and platelet levels remained stable.

DISCUSSION

The most common cause of hemolysis in erythrocytes in newborns is Rh incompatibility, with ABO incompatibility being the second most prevalent cause. (2-4) If autoimmune hemolytic disease is considered in a patient but these conditions are not present, subgroup incompatibility should be considered a potential cause. (10) There are more than 70 known erythrocyte antigens. The minor blood groups most commonly cause incompatibility between mother and baby are C, c, E, e, Kell, Duffy, Diego, Kidd and MNS. (1,3) The most common are anti-Kell, anti-E and anti-c. (7) Anti-E antibody was also detected positive in our case.

In response to antigenic stimulation, the first maternal IgM antibodies are formed. Since these antibodies cannot cross the placenta, they cannot cause sensitization in the fetus. IgG antibodies are formed if antigenic stimulation continues and their titers gradually increase. These antibodies can cause a positive indirect Coombs test in the mother and pass to the fetus thro-

ugh the placenta, causing hemolytic disease in the newborn. (5,7) In the present case, it was learned that the direct Coombs test was positive, and the mother's indirect Coombs test was positive. Findings support the diagnosis of anti-E subgroup incompatibility.

Anti-E subgroup incompatibility can be seen in a vast clinical spectrum. While severe conditions, such as hydrops fetalis and severe anemia, may be observed, only indirect hyperbilirubinemia may also be encountered. (3,5)

Özdemir et al. reported two cases with anti-E subgroup incompatibility. The first case was diagnosed on the second postnatal day after indirect hyperbilirubinemia (total bilirubin: 21 mg/dl) and direct Coombs test 4 positive. The patient was treated with intensive phototherapy and IVIG (1 gr/kg, single dose), and it was reported that no hemolysis complications developed. The other case was investigated after the indirect Coombs test was positive in the mother. The direct Coombs test from the cord blood of the case was determined to be 4 positive. Despite intensive phototherapy, the patient was treated with intravenous immunoglobulin (IVIG) (1 g/kg, single dose) due to a rapid increase in bilirubin levels. Similarly, we applied IVIG treatment to our case in the early period. The patient, discharged on the 4th postnatal day, did not come for regular check-ups. The patient presented with complaints of pallor and jaundice at the age of 33 days. The patient, who developed anemia (Hb: 5 g/dl) and indirect hyperbilirubinemia (total bilirubin: 14,9 mg/dl), was treated with short-term phototherapy, IVIG (1 g/kg, single dose) and erythrocyte transfusion. The patient was discharged and taken under follow-up. Similar anemia was observed during follow-up and subgroup-appropriate erythrocyte transfusion was administered in our case. (7)

Özcan et al. reported a case with anti-E subgroup incompatibility. The direct Coombs test of the patient, whose total bilirubin value was 18,7 mg/dl on the 4th postnatal day, was 4 positive. It was reported that the patient, whose total bilirubin level decreased to 10,8 mg/dl after 28 hours of phototherapy, did not need additional treatment, and no signs of hemolysis developed during follow-up. In this case, the condition seems to be milder, but in our case, hyperbilirubinemia reached serious levels in the first six hours and could not be controlled with phototherapy. (5)

Tanrıverdi et al. reported a case with anti-E subgroup incompatibility and hereditary spherocytosis diagnosed after being hospitalized for phototherapy with a

total bilirubin value of 26.7 mg/dl at the postnatal 7th day. The patient received 1 g/kg single dose IVIG treatment. The case at the exchange transfusion limit was discharged after five days of phototherapy without the need for exchange transfusion. The patient was checked five days after discharge. The patient was readmitted after Hb was determined as 8,7 g/dl and the total bilirubin value was determined as 17 mg/dl. It was reported that the patient was discharged after receiving a subgroup-appropriate erythrocyte transfusion. Similar to our case, hyperbilirubinemia was controlled with phototherapy and IVIG treatment. It is emphasized that anemia secondary to hemolysis may develop, and therefore, follow-up is important. (1)

Karagol et al. detected anti-E subgroup incompatibility in 30 (28.3%) of 106 cases with subgroup incompatibility. Coombs test (direct or indirect) was positive in 33.3% of these patients. The indirect Coombs test was positive in 22.6% of the mothers of 106 cases. Of the cases with anti-E subgroup incompatibility, 60% were followed up with phototherapy, 23.3% with exchange transfusion, 6.6% with IVIG, 6.6% with erythrocyte transfusion and 3.3% with exchange transfusion and IVIG treatment. It was stated that the patient, who received an exchange transfusion and IVIG treatment, had severe birth asphyxia, had low respiratory effort, and died at the age of 12 days. It was stated that two cases presented with hydrops fetalis, and their symptoms improved after the exchange transfusion. In this study, , subgroup incompatibility should be considered in the presence of hemolytic anemia and hyperbilirubinemia even in the absence of Coombs positivity. It has been shown that patients often have mild symptoms and recover only with phototherapy. In the study, it was stated that neonatal anemia improved significantly after subgroup-appropriate erythrocyte transfusion. It has been stated that early IVIG treatment may reduce the need for exchange transfusion. In our case, there was no need for an exchange transfusion after early IVIG treatment and phototherapy. (8)

In conclusion, when ABO and Rh incompatibility are not detected, subgroup incompatibility should be considered in cases of severe hemolytic anemia, severe hyperbilirubinemia or direct Coombs positivity. The significance of close follow-up of cases with subgroup incompatibility regarding late anemia is emphasized.

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Patient Consent Form / Hasta Onam Formu

The parents' of this patient consent was obtained for this study.

Conflict of Interest / Çıkar Çatışması

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