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Case Report

Hyperbilirubinemia due to minor blood group (anti-E) incompatibility in a newborn: a case report

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Abstract

In addition to Rh and ABO incompatibilities subgroup incompatibilities may rarely play a role among the causes of hemolytic anemia and indirect hyperbilirubinemia in newborns. The most common minor blood group antigens that cause blood incompatibility between the mother and baby are C, c, E, e, Kell, Duffy, Diego, Kidd and MNSs antigens. In this article, a newborn in whom hyperbilirubinemia due to anti-E minor blood group incompatibility developed and was treated with phototherapy succesfully is presented and minor blood group incompatibilities due to anti-E are reviewed.

Key words: Anti-E, hyperbilirubinemia, minor blood group incompatibility, newborn

Introduction

The frequency of neonatal hemolytic disease and indirect hyperbilirubinemias related with Rh sensitization has decreased with widespread use of anti-D gamma globulin, and the importance of minor blood group (subgroup) incompatibilities has gradually increased (1, 2).

Some patients with minor blood group incompatibility may be asymptomatic or clinical pictures ranging from active hemolysis to neonatal jaundice requiring exchange transfusion may be observed (2, 3). Minor blood group incompatibilities are responsible of 3-5% of the cases of neonatal hemolytic jaundice (4).

In this case report, a newborn who developed indirect hyperbilirubinemia due to incompatibility of E antigen, which is one of the minor blood groups, is presented because of the rarity of such cases, and minor blood group incompatibilities due to anti-E are reviewed.

Case

A male baby who was born from the third pregnancy of a 32-year-old mother with a gestational age of 32 weeks and two days and a birth weight of 3500 g by ceserean section as the third living child was discharged without any problem two days after delivery. In his prenatal history, it was learned that the mother received levothyroxine treatment in the last trimester of pregnancy because of hypothyroidism. At the follow-up visit on the fourth day after delivery, he presented with jaundice and his bilirubin level, as measured using a transcutaneous bilirubinometer was found as 18.7 mg/dL. Laboratory findings were as follows: total bilirubin: 17.6 mg/dL, direct bilirubin: 0.5 mg/dL, hemoglobin: 15.7 g/dL, white blood cells (WBC): 7730 /mm^3, platelet count: 274,000 /mm^3, blood group: 0 Rh (+), reticulocyte count: 1.56%, and direct Coombs test: (++++). Hemolysis findings or atypical cells were not observed in a peripheral smear. The mother's blood group was found as 0 Rh (+). The minor blood groups of the mother and baby tested to investigate the etiology of hyperbilirubinemia and

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positive direct Coombs test were as follows: mother: C(+) c(+) E(-) e(+) Kell (-), baby: C(+) c(+) E(+) e(+) Kell(-). Indirect Coombs test in the mother and anti-E antibody levels in the mother and baby were positive. Considering the clinical and laboratory findings, a diagnosis of indirect hyperbilirubinemia related with minor blood group incompatibility due to anti-E was made. The patient was treated by applying phototherapy for 28 hours without the need for advanced treatment methods such as intravenous immunoglobulin or exchange transfusion. The serum total bilirubin level was found as 10.8 mg/dL after phototherapy. On the follow-up visit one day after discharge, no "rebound" hyperbilirubinemia was found and pathologic hyperbilirubinemia did not develop in the further follow-up. Verbal informed consent was obtained from the patient's parents.

Discussion

Hemolytic disease of the newborn occurs as a result of hemolysis and shortening of the life span of the newborn's erythrocytes because of antibodies crossing from the mother by the placenta (5). Hemolysis of erythrocytes in the fetus and newborn is most frequently caused by antibodies produced due to Rh and ABO incompatibilities (2). Minor blood group incompatibilities should be considered in cases of hemolytic disease where Rh and ABO incompatibilities cannot be found and with positive Coombs tests (2, 5).

The most common minor blood group antigens that lead to blood incompatibility between the mother and baby include C, c, E, e, Kell, Duffy, Diego, Kidd, and MNSs antigen systems (3). It has been reported that the most severe hemolytic picture is caused by Anti c antibodies (5,6). Although jaundice at a level necessitating exchange transfusion did not develop in our patient, anti-E antibody was found as positive.

The pathophysiology of isoimmunization in minor blood group incompatibility in the fetus and newborn is similar to the pathophysiology of Rh incompatibility. The initial maternal antibodies produced as a response to antigenic stimulus are immunoglobulin (Ig)-M antibodies, but they have no importance in the pathogenesis of hemolytic disease of the newborn because they cannot cross the placenta. However, IgG antibodies increase with further antigenic stimuli and in antigen-positive pregnancies. These antibodies can cross the placenta and may lead to a positive indirect Coombs test in the mother. Thus, they cause hemolytic disease in the fetus and newborn with varying severity (2, 5). In the case presented in this article, the direct Coombs test, indirect Coombs test in the mother, and anti-E antibody levels were positive and the diagnosis of hyperbilirubinemia caused by minor blood group incompatibility due to anti-E was confirmed.

In cases of hemolytic disease due to minor blood group incompatibility, the picture may vary from subclinical hemolysis to active hemolysis and hyperbilirubinemia, which require exchange transfusion (2, 3, 5). Early and severe pictures such as hydrops fetalis (7) or later and mild pictures such as prolonged jaundice (5) may also be observed.

Variability of clinical findings related with minor blood group incompatibility is also valid for blood group E. To et al. (8) reported that serious hyperbilirubinemia did not develop in a newborn whose mother had a positive indirect Coombs test in the screening performed in the 15th week of pregnancy and who had positive anti-E after delivery. On the other hand, Sarıcı et al. (1) reported a newborn who was diagnosed as having hemolytic disease due to anti-E and had severe hyperbilirubinemia that necessitated exchange transfusion twice on the postnatal fourth day (total bilirubin level 36 mg/dL). Onesimo et al. (9) reported that they obtained successful results with phototherapy and intravenous (IV)-IG in E subgroup incompatibility. Our patient was also successfully treated with phototherapy without the need for IVIG or exchange transfusion. This clinical prognosis might have arisen from the relatively mild anti-E hemolytic disease prognosis and/or close and strict follow-up after discharge, which is practiced in our unit. In this way, diagnosis could be made and treatment was administered before the hyperbilirubinemia reached significant levels.

Another finding in our case that directed us to investigations that would confirm the diagnosis was the direct Coombs positivity found during the investigation of the cause of hyperbilirubinemia. In minor blood group incompatibilities, the rate of direct Coombs test positivity is generally 33% (2, 5, 10). It should be kept in mind that a direct Coombs test may be positive (3) or negative (2, 7) in E blood group incompatibilities.

In conclusion, physicians should consider that minor blood group incompatibilities may be involved in the etiology of newborns who present with jaundice and have a positive direct Coombs test.

Informed Consent: Verbal informed consent was obtained from patients' parents who participated in this case.

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