Prenatal Diagnosis of Maternal-Fetal Blood Subgroup Antigen Incompatibility Due to C Antigen: A Case Report

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In this paper, we report a case of materno-fetal C-subgroup incompatibility that was managed at our institution. A 41-year-old woman was admitted to our prenatal outpatient unit for the first time at 29th week of a singleton pregnancy. After an indirect coombs test result of 1/64 positive, cordocentesis was performed. Fetal blood group was reported as AB Rh(-), and Direct coombs test was reported to be +3 positive. A 3040 gr live fetus was delivered by cesarean section, on the 34th week of pregnancy. Maternal blood samples revealed C(-), c(4+), E(-), e (4+) and Kell (-), and the fetus had direct coombs 3+, C(4+), c(3+), E (-), e (4+) and Kell (-). No fetal complications occurred.

Key Words: Alloimmunization, Subgroup incompatibility, C-antigen, Fetal hydrops

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Introduction

Hemolytic disease of the newborn carries significant risk for fetal hyperbilirubinemia, which is an important etiologic factor for bilirubin encephalopathy. In the newborn period, numerous blood group systems have been linked with fetal hemolysis.[1,2] There is currently no consensus on the appropriate management of Kell, C, c, E, and e subgroup incompatibilities. We present a case of maternofetal C subgroup incompatibility that was managed at our institution.

Case Report

A 41-year-old gravidity 7, parity 2 woman with two prior cesarean sections was admitted to our prenatal outpatient unit for the first time at 29th week of a singleton pregnancy. The blood groups and Rh types of the patient and her spouse were A Rh (-) and B Rh (+), respectively. On her initial visit, indirect coombs test was reported positive with a titer of ½. She did not report any vaginal bleeding, abdominal trauma, history of blood transfusion or invasive interventions in the current pregnancy. On her second visit five days later, indirect coombs test was 1/64 positive. On ultrasonography, normal fetal biometric measurements were obtained, without any signs of fetal hydrops. On obstetric Doppler examination, middle cerebral artery (MCA) Doppler peak systolic velocimeter measurements were also in the normal range. Cordocentesis performed on the same day, with a preliminary diagnosis of affected maternal-fetal blood group incompatibility. Fetal blood group was reported as AB Rh (-). Fetal hemoglobin and hematocrit levels were 14.0 gr/dl and 43%, respectively. Direct coombs test was reported to be +3 positive. As there was no fetal anemia, close follow-up was planned. On the 34th week of pregnancy, the patient was admitted to our emergency department with regular uterine contractions. Ultrasonographic fetal biometric measurements were compatible with the gestational age, and again, no signs of fetal hydrops were detected. Indirect coombs test was positive with a titer of 1/128. A 3040 gr live fetus was delivered by cesarean section with 1st and 5th minute APGAR scores of 5 and 8, respectively. Detailed fetal and maternal blood subgroup antigen analyses were performed. Maternal blood samples revealed C (-), c (4+), E (-), e (4+) and Kell (-). The fetus had direct coombs 3+, C (4+), c (3+), E (-), e (4+) and Kell (-). Incompatibility was detected only for C antigen. Newborn's hemoglobin and hematocrit values were 16 gr/dl and 46%, respectively. Newborn's peripheral blood smear showed: normoblasts to be 20-25 % and high corrected reticulocyte count to be 13%. At the postnatal 6th hour analysis, total bilirubin was 4.3 mg/dl. The baby was immediately started on a course of conventional phototherapy.

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Moreover, 1 mg/kg IVIG therapy was instituted for hemolysis due to C subgroup incompatibility. On postnatal period, bilirubin and hemoglobin levels were stabilized, and the fetus was discharged uneventfully.

Discussion

Maternal alloimmunization due to minor red cell antigens is one of the major causes of fetal and neonatal hemolytic disease, since no prophylactic immunoglobulins are available to prevent antibody formation.[3]

The C antigen group was initially considered to be expressed together on the C/c locus. However, it was discovered recently that each antigen can be expressed in the absence of the other. C antigen is found in about 2 percent of caucasians and very rare in black population.[4] Karagol et al, in their study have reported C subgroup incompatibility to be 37.7% of their study population.[5] Geifman-Holtzman et al. reported the frequencies as 22% for Kell, 18.4% for D, 14% for E,5.8% for c, and 4.7% for C subgroup incompatibilities[6]

Positive direct antiglobulin test on cord RBCs has been reported in the hemolytic disease of the newborn due to irregular subgroup incompatibilities.[7] However, positive fetal or neonatal direct Coombs test does not necessarily correlate with the severity of hemolytic disease[8] In addition, Coombs test may be negative in the case of small subgroup antibody titers. This negative result does not exclude red cell sensitization. Although the reason for this negativity is unknown, a weak antigen-antibody interaction or intravascular hemolysis is proposed as the possible explanation by some of the authors.[9] Immune hydrops results from maternal antibodies that are capable of crossing the placenta to react with fetal antigen, thus causing a reaction that manifests as fetal hemolysis. Severe fetal hemolysis can result in fetal hydrops. When isoimmunization was identified as the cause, RhD antigens were responsible for 4.2% of cases. There were only two cases due to non-RhD antigens, one each due to Kell and to Duffy. [10] Cases with hydrops fetalis due to C and c subgroup incompatibilities were even less frequent in the literature.[11]

The treatment of anemia in subgroup isoimmunizations associated with other irregular RBC antibodies is similar to the management of anti-D isoimmunized pregnancies, with the exception that blood used for fetal and/or neonatal transfusion should be negative for its respective antibodies. There are only few reports where IVIG was administered in hemolytic disease of newborn due to subgroup incompatibility.[11] Although the exact mechanism of action of IVIG is still unknown, it is thought to exert its effect mainly through Fc receptor blockade of the reticuloendothelial system. IVIG therapy was shown to reduce the need for exchange transfusions in babies with RhD and ABO hemolytic diseases.

To conclude, minor group antibody screening is recommended both in the mother and the high-risk infants with hydrops and any suspicion of fetal anemia.

Delayed recognition of both hemolysis and hyperbilirubinemia in neonates should be prevented, and early diagnosis and interventions should not be delayed.

C - Antijenine Bağlı Maternal-Fetal Subgroup Uyuşmazlığının Prenatal Tanısı: Olgu Sunumu

Bu makalede, kurumumuzda tanı alan ve tedavi edilen bir maternofetal C-subgrup uyuşmazlığı olgusu sunulmaktadır. Kırk bir yaşındaki bir hasta, prenatal takip ünitemize ilk olarak gebeliğin 29. haftasında başvurdu. İndirekt coombs testinin 1/64 pozitif gelmesi üzerinde kordosentez yapıldı. Fetal kan grubu AB Rh (-) olarak raporlandı, ayrıca direct coombs testi 3+ idi. Gebeliğin 34. haftasında 3040 gram canlı fetus sezaryenle doğurtuldu. Maternal ayrıntılı kan gruplamasında C (-), c (4+), E (-), e (4+) ve Kell (-) iken, fetüsün direkt coombs testi 3+, C (4+), c (3+), E (-), e(4+) and Kell (-) idi. Fetal komplikasyon gelişmedi.

Anahtar Kelimeler: Alloimmünizasyon, Subgroup uyuşmazlığı, C-antijeni, Fetal hidrops

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