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Case Report

Neonatal hyperbilirubinemia due to minor group (c antigen) incompatibility

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Abstract

Background: A male neonate born at 37+4 weeks of gestation with a birth weight of 2.94 kg, cried immediately at birth, and was admitted to the Neonatal intensive care unit (NICU) soon after birth in view of antenatally detected positive indirect coombs test (ICT). At admission, baby had normal vital signs and systemic examination. The baby was pink without pallor and icterus. Cord blood investigations for hemolysis workup revealed elevated total bilirubin with low hemoglobin, elevated retic count and positive direct coombs test. The mother's and baby's blood group were B negative and AB positive, respectively. Double volume exchange transfusion was performed under strict aseptic condition and intensive phototherapy was given. A repeat haemolytic workup done at 36 hours of life reported positive DCT, low hemoglobin and elevated retic count and significant rise of bilirubin. Two doses of Intravenous immunoglobulin (IVIG) was administered in view of ongoing hemolysis and worsening hyperbilirubinemia. In view of persistent hemolysis, the baby's blood was tested for minor blood group incompatibility which revealed strongly positive anti-C antibodies. On day 8 of life, hemolytic workup was repeated which reported positive DCT (2+ compared to previous 4+), improved hemoglobin and normal bilirubin levels. On day 12 of life, hemolytic workup was normal. This established the diagnosis of anti-C hemolytic disease. On day 29 of life, hemolytic workup done on OPD basis reported low hemoglobin (8.2 g/dL) and positive DCT for which the infant was admitted, IVIg and PRBC transfusion was done in view of anaemia (Hb-8.2 g/dL). Subsequently, the parameters were normal. Currently, the infant is on follow-up and asymptomatic. Anti-C minor blood group incompatibility should be considered in the setting of hemolysis and persistent hyperbilirubinemia due to isoimmunization in neonates. Timely diagnosis and management can avert morbidity and mortality.

Keywords: Neonate, Hemolytic disease, Hyperbilirubinemia, Minor group incompatibility, Exchange transfusion

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1. Introduction

Hemolytic disease of the fetus and newborn (HDN) is a disease that is caused by maternal alloantibodies to the fetal red blood cells. It occurs due to an incompatibility between the fetal/neonatal and maternal blood, leading to the destruction of fetal/neonatal red blood cells (RBCs) and resulting in hyperbilirubinemia during the neonatal period. The primary causes of HDN include ABO and Rh incompatibilities, which are responsible for clinically significant hyperbilirubinemia. In addition to these common causes, subgroup incompatibilities contribute to 3-5% of all cases of neonatal jaundice.[1] The importance of minor blood group incompatibilities has increased in the etiology. The most frequently encountered subgroup incompatibilities involve non-D Rh antigens (c, C, E, e), Kell, Duffy, Kidd, and MNS antigens. These incompatibilities can range from mild, subclinical hemolysis to severe hemolysis, which may necessitate an exchange transfusion. The incidence of HDN due to subgroup mismatches has been rising significantly. The incidence of subgroup incompatibilities are anti-D 18.4%, anti 14%, anti-C 4.7%, anti-Kell 22%, anti-MNS 4.7%, Duffy 5.4%, and JKa 1.5%. Children with minor blood group incompatibility may present with a range of clinical symptoms, from subclinical hemolysis with mild laboratory abnormalities to active hemolysis with severe jaundice, anemia, and potentially life-threatening complications. Symptoms may include pallor, lethargy, and

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jaundice, which can appear within the first 24-48 hours of life. Laboratory findings may reveal elevated indirect bilirubin, lactate dehydrogenase (LDH), and reticulocyte count, with decreased hemoglobin and hematocrit. In severe cases, active hemolysis can lead to heart failure, kernicterus, and neurological damage, emphasizing the importance of early detection and treatment. Anti-C antibodies may occur due to exposures, such as fetomaternal hemorrhage, abruptio placentae, spontaneous or therapeutic abortion, cesarean delivery, ectopic pregnancy or transfusion. This article discusses a case of a newborn with 'c' subgroup incompatibility, who presented with clinical signs of hemolysis, including anemia, hyperbilirubinemia, and a positive direct Coombs test. The condition was managed with double volume exchange transfusion, intensive phototherapy, and intravenous immunoglobulin (IVIG).[2]

2. Case Details

A male neonate born at 37+4 weeks of gestation with a birth weight of 2.94 kg, cried immediately at birth, and was admitted to the Neonatal intensive care unit (NICU) soon after birth given antenatally detected positive indirect coombs test (ICT). At admission, the baby had normal vital signs and a systemic examination. The baby was pink without pallor and icterus. Cord blood investigations for hemolysis workup revealed elevated total bilirubin (1.9 mg/dL) and indirect bilirubin (1.2 mg/dL) with low hemoglobin (10.3 gm/dL), elevated retic count (6.2%) and strongly positive (4+) direct coombs test (DCT). Peripheral blood smear was suggestive of hemolysis. The mother's and baby's blood groups were B negative and AB positive, respectively. Double volume exchange transfusion was performed under strict aseptic condition and intensive phototherapy was given. A repeat hemolytic workup done at 36 hours of life reported positive DCT, low hemoglobin (9.6 gm/dL) and elevated retic count (5.5%) and significant rise of bilirubin (Total 2.9 mg/dL, indirect 2.4 mg/dL). Two doses of Intravenous immunoglobulin (IVIG) were administered given ongoing hemolysis and worsening hyperbilirubinemia.

Despite persistent hemolysis, the baby's blood was tested for minor blood group incompatibility, revealing strongly positive anti-C antibodies. Mother was negative for C antigen and father was strongly positive for anti-C antibodies. On day 8 of life, hemolytic workup was repeated which reported positive DCT (2+ compared to previous 4+), improved hemoglobin (11.3gm/dL), low retic count (0.6%) and normal bilirubin levels. On day 12 of life, hemolytic workup was repeated which reported weakly positive DCT and other parameters were normal. This established the diagnosis of anti-c haemolytic disease due to minor blood group c incompatibility as a cause of hyperbilirubinaemia in neonates. On day 29 of life, hemolytic workup was done on OPD basis reported low hemoglobin (8.2 g/dL) and positive DCT for which the infant was admitted, IVIg and PRBC transfusion was done in view of anemia (Hb-8.2 g/dL). Subsequently, the parameters were normal. Currently, the infant is on follow-up and asymptomatic.

3. Discussion

Minor blood group incompatibilities account for 3-5% of cases of hemolytic jaundice in newborns. Anti-C alloimmunization, sometimes accompanied by anti-E, is found in 0.07% of all pregnancies, with few reported cases involving Rh antibodies other than anti-D. Incompatibilities involving minor blood groups, other than anti-D, are often underreported and frequently misdiagnosed. When a newborn presents with signs of hemolysis, such as a positive direct agglutination test and hyperbilirubinemia, and no Rh or ABO incompatibility is identified, it may indicate the possibility of a minor blood group incompatibility. This case report highlights how hemolytic disease of the fetus and newborn (HDFN) caused by minor blood group incompatibility, other than the D antigen, can range from moderate to severe. The reported neonate required exchange transfusion. Antibody screening during pregnancy is essential, as Rh(D) positive women face the same risk of developing alloantibodies as Rh(D) negative women. Subgroup mismatch should always be kept in mind for newborns presenting with severe hemolytic anemia, and requiring exchange transfusion. Additional and sustained efforts should be made to prevent under-reporting of events and to improve data comparability.[3]

Minor blood group incompatibilities, other than anti-D, remain underreported and often misdiagnosed. These incompatibilities can present as either asymptomatic or with severe hyperbilirubinemia and kernicterus. Early detection of significant antibody titers in the mother, before delivery, is crucial for managing at-risk newborns, preventing substantial morbidity and mortality.[4] Anti-c minor blood group incompatibility should be considered in cases of hemolysis and persistent hyperbilirubinemia due to isoimmunization in neonates, particularly when Rh and ABO incompatibilities are excluded.[5] Timely diagnosis and intervention can prevent serious outcomes.[6]

4. Conclusion

Anti-c minor blood group incompatibility should be considered in cases of hemolysis and persistent hyperbilirubinemia due to isoimmunization, particularly when Rh and ABO incompatibilities have been excluded. Early detection of significant antibody titers in the mother, before delivery, is crucial for managing at-risk newborns, preventing substantial morbidity and mortality.

5. Sources of Funding

None.

6. Conflict of Interest

None.

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