Original Research Paper

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HEMOLYTIC DISEASE OF THE NEWBORN DUE TO COMBINED MINOR RH (ANTI-c AND ANTI-E) ISOIMMUNIZATION IN A LATE-PRETERM NEONATE COMPLICATED BY LATE-ONSET SEPSIS: A CASE REPORT

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ABSTRACT Hemolytic disease of the newborn (HDN) is most commonly caused by Rh-D incompatibility; however, minor Rh antibodies such as anti-c and anti-E can also result in clinically significant hemolysis, even in Rh-positive mothers, and often pose diagnostic and transfusion challenges. We report the case of a late-preterm male neonate, born to an O-positive mother, who developed persistent unconjugated hyperbilirubinemia and progressive anemia despite adequate phototherapy. The clinical course was further complicated by late-onset neonatal sepsis, which initially masked the underlying hemolytic process. Neonatal immunohematology workup showed a strongly positive direct antiglobulin test (4+) and a positive autocontrol (3+), with antibody identification suggesting anti-c and antigen typing confirming a c-positive phenotype; the presence of a concomitant anti-E antibody could not initially be excluded, and extended workup on a maternal sample was requested. Maternal testing, performed as she was c-negative and E-negative, confirmed both anti-c and anti-E antibodies, establishing a diagnosis of hemolytic disease of the newborn due to combined minor Rh (anti-c and anti-E) isoimmunization. The neonate was managed successfully with antigen-negative packed red blood cell transfusion, continued phototherapy, and targeted antibiotic therapy, with stabilization of hemoglobin and gradual resolution of jaundice. This case underscores the need to consider combined minor Rh isoimmunization in neonates with unexplained persistent jaundice and anemia, particularly when the mother is Rh positive, and highlights the essential role of direct antiglobulin testing and extended cross-matching, including maternal antibody workup, in reaching a timely and complete diagnosis.

KEYWORDS : Hemolytic disease of the newborn; Anti-c antibody; Anti-E antibody; Minor Rh incompatibility; Neonatal anemia; Persistent jaundice.

INTRODUCTION

Hemolytic disease of the newborn (HDN) results from maternal alloimmunization against fetal red blood cell antigens. Although anti-D antibodies remain the most frequent cause, sensitization to non-D antigens of the Rh system is increasingly recognized due to the widespread use of Rh-D immunoprophylaxis. Among these, anti-c antibodies are clinically the most significant after anti-D and can lead to severe neonatal anemia and hyperbilirubinemia. Early diagnosis is crucial, as routine antenatal antibody screening often fails to detect minor Rh antibodies, particularly in Rh-positive mothers.[1,2].

CASE REPORT

A late-preterm male neonate, born to a 26-year-old G2P1L1 mother by lower-segment cesarean section, was admitted to the neonatal intensive care unit with respiratory distress soon after birth. The marriage was non-consanguineous, and the mother had an uneventful antenatal course except for hypothyroidism diagnosed in the third month of amenorrhea, for which she was on regular treatment. Both the mother and neonate had blood group O positive.

The baby was delivered at 36 weeks and 1 day of gestation with a birth weight of 2.4 kg. Apgar scores were 6 at 1 minute and 9 at 5 minutes. The baby cried immediately after birth but subsequently developed respiratory distress characterized by subcostal retractions and grunting, with a Silverman-Anderson score of 4. Chest radiograph showed features suggestive of respiratory distress syndrome. The neonate was initially supported with CPAP and received surfactant via the INSURE technique, following which CPAP was continued. Empirical intravenous antibiotics (piperacillin-tazobactam and amikacin) were started after sending a sepsis screen, in accordance with standard neonatal care protocols[3].

On postnatal day 4, the baby developed clinical jaundice involving the palms and soles. Total serum bilirubin was 19.5 mg/dL, above the phototherapy threshold, and double-surface phototherapy was initiated and continued for 48 hours. Peripheral smear at this time showed normocytic normochromic anemia.

Despite adequate phototherapy, jaundice persisted. On day 7 of life, repeat investigations revealed a fall in hemoglobin from 12.5 g/dL to 10.2 g/dL, thrombocytopenia, and rising CRP levels, with a positive blood culture, following which antibiotics were upgraded, confirming late-onset neonatal sepsis. Coagulation profile and reticulocyte count were within normal limits, suggesting anemia secondary to marrow suppression due to sepsis at that point[3].

In view of persistent jaundice and falling hemoglobin levels, packed red blood cell transfusion was planned; however, repeated incompatible cross-matching raised suspicion of immune-mediated hemolysis. Advanced immunohematology workup on the neonate's sample showed a strongly positive direct antiglobulin test (DAT, 4+) and a positive autocontrol (3+), confirming antibody-mediated hemolysis. Antibody identification suggested anti-c, and appropriate antigen typing confirmed a c-positive phenotype on the neonate's red cells; the report noted that a concomitant anti-E antibody could not be excluded on the neonatal sample alone, and testing of a maternal sample was requested for confirmation (Fig. 1). Subsequent peripheral smear demonstrated normocytic normochromic anemia with occasional schistocytes, consistent with hemolysis[1,2].

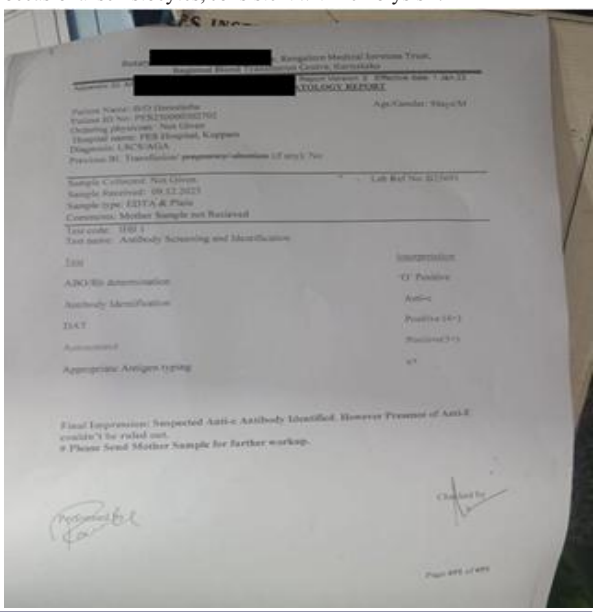
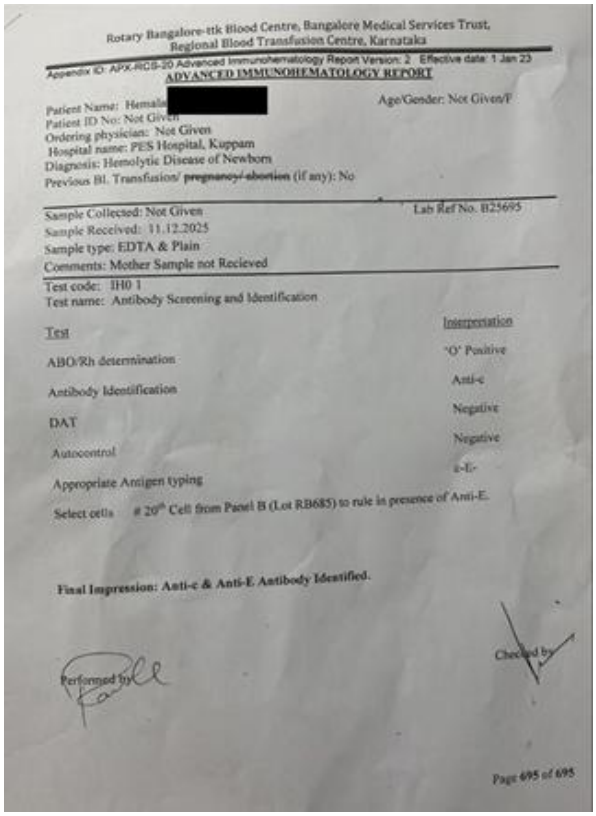


Fig. 1: Advanced immunohematology report of the neonate (sample received day 9 of life) showing DAT 4+, autocontrol 3+, and antibody identification suggestive of anti-c, with anti-E not excluded. Patient identifiers redacted.

Extended immunohematology workup on the maternal sample showed the mother to be group O positive with a c-negative, E-negative red cell phenotype, and antibody identification confirmed both anti-c and anti-E antibodies in her serum (Fig. 2), consistent with transplacental transfer of maternal antibodies to the fetus. A diagnosis of hemolytic disease of the newborn due to combined minor Rh (anti-c and anti-E) isoimmunization was established[1].



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Appendix ID: APX-RCB-20 Advanced Immunohematology Report Version: 2 Effective date: 1 Jan 23

ADVANCED IMMUNOHEMATOLOGY REPORT

Patient Name: Hemala[redacted] Age/Gender: Not Given/F
Patient ID No: Not Given
Ordering physician: Not Given
Hospital name: PES Hospital, Kuppam
Diagnosis: Hemolytic Disease of Newborn
Previous Bl. Transfusion/ ~~pregnancy/ abortion~~ (if any): No

Sample Collected: Not Given Lab Ref No. B25695
Sample Received: 11.12.2025
Sample type: EDTA & Plain
Comments: Mother Sample not Recieved

Test code: IH0 1
Test name: Antibody Screening and Identification

Test	Interpretation
ABO/Rh determination	'O' Positive
Antibody Identification	Anti-c
DAT	Negative
Autocontrol	Negative
Appropriate Antigen typing	c-E-

Select cells # 20th Cell from Panel B (Lot RB685) to rule in presence of Anti-E.

Final Impression: Anti-c & Anti-E Antibody Identified.

Performed by Checked by

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Fig. 2: Advanced immunohematology report of the mother, confirming a c-negative, E-negative phenotype and identification of both anti-c and anti-E antibodies. Patient identifier redacted.

The baby received antigen-negative packed red blood cell transfusion following extended cross-matching, along with continued phototherapy and targeted antibiotics. The baby showed clinical improvement, with stabilization of hemoglobin levels and gradual resolution of jaundice.

DISCUSSION

The Rh blood group system is one of the most immunogenic systems in humans, comprising more than 50 antigens, of which D, C, c, E, and e are clinically most significant. The D antigen accounts for nearly 50% of maternal alloimmunization[2]. Rh alloantibodies such as anti-C, anti-E, and anti-e are usually associated with mild disease; however, anti-c, especially when combined with anti-E, can result in severe fetal anemia and neonatal hemolytic disease[1,2].

Persistent jaundice despite adequate phototherapy, progressive anemia, repeated minor cross-match incompatibility, and a strongly positive direct Coombs test were crucial clues suggesting immune-mediated hemolysis. Importantly, anemia due to sepsis alone does not cause direct Coombs test positivity, emphasizing the need to consider immune hemolysis even in sick neonates[3].

Management of anti-c isoimmunization is similar to that of anti-D incompatibility, with the essential requirement that transfused blood be negative for the corresponding antigen. Therefore, routine antenatal screening for irregular antibodies, even in Rh-positive mothers, is necessary for early diagnosis and prevention of severe HDN[1,3].

CONCLUSION

This case highlights the importance of suspecting minor Rh incompatibility in neonates presenting with persistent jaundice and unexplained anemia, even when the mother is Rh positive. Direct Coombs testing and extended cross-matching are indispensable diagnostic tools, and early identification with timely transfusion of antigen-negative blood can be life-saving[1,3].

REFERENCES

1. Sheeladevi CS, Suchitha S, Manjunath GV, Murthy S. Hemolytic disease of the newborn due to anti-c isoimmunization: A case report. Indian J Hematol Blood Transfus. 2013;29(3):155-157.
2. Avent ND, Reid ME. The Rh blood group system: a review. Blood. 2000;95(2):375-387.
3. Kliegman RM, St Geme JW, Blum NJ, Shah SS, Tasker RC, Wilson KM. Hemolytic disease of the fetus and newborn. In: Nelson Textbook of Pediatrics. 21st ed. Philadelphia: Elsevier; 2020. p. 1036-1040.