

Access this article online

Quick Response Code:



Website:
www.ajts.org

DOI:
10.4103/ajts.AJTS_21_17

A rare case of hemolytic disease of newborn due to weak D (D unknown) antigen in child

Nirav Ramesh Dava, Alok Upadhyaya, Neha Agarwal, Amarjeet Mehta, Vijaypal Choudhary, Gourav Goyal

Abstract:

We are reporting a rare case of hemolytic disease of newborn with weak D antigen in child. A 3rd order male child of G₃P₃A₀ mother was admitted at 8th h of life with jaundice. Blood group of both mother and child were A Rh D negative. Baby's direct coombs test was positive. Weak D antigen was positive in baby. Hematological parameters showed all the signs of ongoing hemolysis, and the bilirubin level was in the zone of exchange transfusion. Exchange transfusion was done. An intravenous immunoglobulin was given to child after that. Mother had a history of first normal healthy male child with O Rh D positive blood group. Second male child expired on 3rd postnatal day due to bilirubin encephalopathy that had A Rh D negative blood group with positive direct coombs test.

Keywords:

Blood grouping, D^u antigen, hemolytic disease of newborn, weak D antigen

Introduction

The incidence of weak D antigen ranges between 0.2% and 1% in Caucasians.^[1] Weakly reacting D antigen was described by Stratton in 1946.^[2] The current preferred term for D^u is "weak D."^[3] Weak D red cells have the D antigen but have fewer D antigen sites per red cell than normal Rh positive cells. The difference between D and D^u antigen is that the latter is weakly immunogenic and difficult to detect. Race *et al.* in 1948 and Renton and Stratton in 1950 found that D^u red cells were not agglutinated directly by anti-Rh (D) serum, but required subsequent ant globulin addition to show the presence of this antigen.^[4] There are only few reported case of hemolytic disease of newborn (HDN) with weak D antigen in child.

Case Report

We received a Hindu male child born out of nonconsanguineous marriage with jaundice

at 8th h of life. The child was referred from another hospital. Mother was 25-year-old with A Rh D negative blood group. Father's blood group was O Rh D positive. Mother had a history of the first normal healthy male child with O Rh D positive blood group. Anti-D was given to mother within 24 h of delivery of the first child. Second term male child expired on 3rd postnatal day due to bilirubin encephalopathy (serum total bilirubin was 35 mg/dl) who had A Rh D negative blood group with positive direct coombs test. Anti-D was again given to mother within 24 h of delivery of second child. In her third pregnancy, she remained in regular antenatal checkup. In 2nd trimester of 3rd pregnancy, her Rh D antibody titer was 1:32 (positive) and indirect coombs test was positive. Again anti-D was given within 24 h delivery of third child. Baby was born by normal vaginal delivery with APGAR score 8 at 5 min. Breastfeeding was initiated within 30 min of birth. Doctors noticed icterus at 5th h of life so baby was

Department of Paediatrics,
SMS Medical College and
Attached J K Lon Hospital,
Jaipur, Rajasthan, India

Address for correspondence:

Dr. Nirav Ramesh Dava,
Department of Paediatrics,
SMS Medical College
and Attached J K Lon
Hospital, Jaipur - 302 017,
Rajasthan, India.
E-mail: niravdava@gmail.com

Submission: 13-02-2017

Accepted: 14-08-2017

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Dava NR, Upadhyaya A, Agarwal N, Mehta A, Choudhary V, Goyal G. A rare case of hemolytic disease of newborn due to weak D (D unknown) antigen in child. Asian J Transfus Sci 2018;12:75-7.

referred to our institute. The child was admitted in our hospital at 8th h of life with icterus upto chest. Vitals were stable, and neurological examination was normal. The weight of this male child was 2.7 kg and blood group was A Rh D negative. At 12th h of life, baby's hemoglobin was 10.8 g%, hematocrit was 32.8%, serum total bilirubin was 10.6 mg/dl, and serum indirect bilirubin was 9.82 mg/dl, corrected reticulocytes count was 2.5%. Peripheral smear showed anisocytosis. Direct coombs test was positive (+2). There was no ABO and minor blood group incompatibility. G6PD (Glucose-6-phosphate dehydrogenase) level was normal. Patient was subjected for TORCH profile, osmotic fragility test, high-performance liquid chromatography, and thyroid profile. Reports of all these tests were normal. All findings were suggestive of neonatal jaundice due to HDN. Double surface light-emitting diode phototherapy was started. At 30th h of life, baby's hemoglobin was 10.5 g% with 33.8% hematocrit. Serum total bilirubin was 18.61 mg/dl, and indirect bilirubin was 17.05 mg/dl. Double volume exchange transfusion was done with O Rh D negative blood group at 36th h of life. After exchange transfusion, a dose of human intravenous immunoglobulin (1 g/kg) was given. Phototherapy was continued for the next 72 h. At 6th day of life, hemoglobin was 14.1 g%, serum total bilirubin was 9.56 g%, and serum indirect bilirubin was 9.14 mg/dl. That time direct coombs test was negative. The patient was discharged in a healthy condition on the 10th postnatal day with serum total bilirubin 3.1 g/dl and hemoglobin 13.9 g%. As there was no apparent cause of the hemolytic disease of newborn, further investigation was done with samples preserved before exchange transfusion. There was a weak D (D unknown) antigen in baby which was the cause of hemolytic disease of newborn.

Discussion

Weak D is defined as the weakened expression of the normal D antigen. Missense mutations observed in the alleles of all weak D types have been demonstrated to be the probable cause for the reduced D antigen expression.^[5]

Due to weakened expression of the normal D antigen, these cells require additional steps to test the D antigen which may be prolonged incubation with the anti D reagent or addition of ant globulin serum after incubation with anti D. Monoclonal anti-D reagents may cause direct agglutination of some D-positive cells that would have been considered weak D after the use of polyclonal reagents.

Two genes, the RHD and RHCE encode the antigens of Rh blood group. It is generally believed that

weak D phenotype could arise from three different genetic mechanisms.

1. A person may inherit an RHD gene which codes for a weakly expressed D antigen
2. D antigen may be weakly expressed due to the presence of C antigen in the transposition on the opposite chromosomes such as Dce/dCe genotype
3. When one or more epitopes of the D antigen are missing, a weak D phenotype may be seen.^[6]

The incidence weak D antigen ranges between 0.2% and 1% in white Caucasians.^[1] Makroo *et al.* studied in Indian population and found Rh negativity in 7.19% and weak D in 0.01% population.^[7]

There are only few reports of HDN in babies with weak D antigen in literature. Lacey *et al.* reported a case of HDN due to anti-D in an Rh-positive D^u variant mother.^[8]

Two cases of infants with Rhesus D^u incompatibility in the Rh negative mothers but without showing evidence of HDN were reported by Dias *et al.* and Perez *et al.*^[9,10] Perez *et al.* found no significant evidence of hemolytic disease of the newborn in infant due to their depressed monocyte-macrophage function.^[10]

There are more than 50 types of weak D antigen. The majority (90%) of individuals with a weak D phenotype is weak D type 1, 2, or 3 and expresses normal, but reduced quantities of D antigens on the red blood cell surface; these individuals cannot be immunized to make anti-D. These individuals do not need Rh immune globulin prophylaxis during pregnancy. The remaining 10% of individuals with a weakened expression of D express aberrant D proteins so they should receive Rh immune globulin prophylaxis during pregnancy.^[11]

Our case demonstrates a D negative mother with a weak D positive infant. Since pregnancy can be a sensitizing event, it is recommended that weak D testing be performed on cord samples from infants who type as D negative directly born to D negative mothers.

Due to poor financial condition of parents, we could not classify the subtypes of weak D antigen and role of phagocytic function of the newborn's monocyte-macrophage in hemolytic disease of newborn.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in

the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Urbaniak SJ, Robertson AE. A successful program of immunizing Rh-negative male volunteers for anti-D production using frozen/thawed blood. *Transfusion* 1981;21:64-9.
2. Stratton F. A new Rh allelomorph. *Nature* 1946;158:25.
3. Brecher ME. *Technical Manual*. 15th ed. Bethesda MD: American Association of Blood Banks; 2005
4. Race RR, Mourant EE, Lawler SD, Sanger R. The Rh chromosome frequencies in England. *Blood* 1948;3:689-95.
5. Wagner FF, Gassner C, Müller TH, Schönitzer D, Schunter F, Flegel WA. Molecular basis of weak D phenotypes. *Blood* 1999;93:385-93.
6. Tippet P. Subdivisions of the Rh antigen D, review. *Med Lab Sci* 1988;45:88-891.
7. Makroo RN, Raina V, Chowdhry M, Bhatia A, Gupta R, Rosamma NL. Weak D prevalence among Indian blood donors. *Asian J Transfus Sci* 2010;4:137-9.
8. Lacey PA, Caskey CR, Werner DJ, Moulds JJ. Fatal hemolytic disease of a newborn due to anti-D in an Rh-positive Du variant mother. *Transfusion* 1983;23:91-4.
9. Dias R, Finney RD, Humphreys D, Graham L. Rhesus Du incompatibility in a newborn with high levels of anti D and a benign clinical course. *Vox Sang* 1986;50:52-3.
10. Pérez D, Cohen DW, Shulman IA, Branch DR. Rhesus Du incompatibility in a newborn without hemolytic disease: A possible role for the mononuclear phagocyte system in the benign clinical course. *Vox Sang* 1986;51:341-3.
11. Eder AF. Update on HDFN: New information on long-standing controversies. *Immunohematology* 2006;22:188-95.