Case Report

Haemolytic Disease of the Newborn

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Abstract

Background: *Immune-mediated haemolytic disease of the newborn refers to a specific category of haemolytic anaemia that results from transplacental passage of IgG antibodies from a pre-sensitized mother to her fetus in utero. This occurs due to blood group incompatibility between the mother and the fetus. The clinical presentation covers a wide spectrum spanning from still births and erythroblastosis fetalis as well as infants born with only mild haemolysis to those having severe anaemia snd severe indirect hyperbilirubinaemia followed by hydrops.*

Objective: *We describe the journey of a Rh-D negative mother who endured through six pregnancies in order to have a healthy baby.*

Conclusion: *To highlight the importance of blood grouping and Rh typing during the first antenatal visit and subsequent monitoring of antibody titers, especially in a mother who is Rh-D negative.*

Key words: *Rh-D incompatibility, Rh isoimmunization, Anti-D titre, Haemolytic disease, Rh antibody titre*

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Introduction

Haemolytic disease of the newborn (HDN) is a condition of premature destruction of red blood cells (RBC) of fetus in uteri and newborns during early neonatal period. This can be immune or non-immune mediated. The commonest underlying reason of the former is transplacental passage of IgG Antibodies produced by sensitized mother and directed against Rhesus, ABO or other antigens on fetal RBCs. Of these, Isoimmunization with Rh-D antigen causes the most severe form of HDN. A history of previously affected fetus or infant in Rh-D negative mother predicts a high chance of similar or greater morbidity in future pregnancies with Rh-positive foetus.[1]

HDN was first described in 1609 in a set of twins by a French midwife: the first twin was hydropic and stillborn, and the second was deeply jaundiced and subsequently died of what we now call kernicterus[2] but established in 1939 by Levine and Stetson. They reported a transfusion reaction from transfusing the husband's blood to a postpartum woman who had been immunized through a feto-maternal hemorrhage.[3] Rh-D haemolytic disease, ABO haemolytic disease and haemolytic disease due to alloantibodies other than anti-D comprise the complete spectrum of HDN.

Objective

In this study, we report a case of a non-pregnant woman who wants to conceive a healthy baby after six previous attempts and what could have been done in previous pregnancies as well as what can be done in the future to fulfil her wish.

Case Presentation

A 35 years old Bangladeshi female, non-hypertensive, non-diabetic was referred to the Department of Transfusion Medicine of Khwaja Yunus Ali Medical College & Hospital, Sirajganj with the blood group AB negative (AB-). Her nonconsanguineous husband had a blood group A positive (A+). She got married in the year 2000 and from the next year she started conceiving. The obstetric history revealed her to be of sixth gravida.

Her second baby was born in 2002 through normal vaginal delivery and is alive but suffers from permanent disability for which he is not under treatment anymore. Two of her

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pregnancies culminated in still births (first and sixth), one pregnancy resulted in intrauterine death (fourth) and the rest two pregnancies ended in the death of neonates due to hyperbilirubinaemia. Unfortunately, as this lady came from a poor socio-economic status and rural background, she did not receive proper antenatal check up in any of her pregnancies.

Table I: Details of all the pregnancies

No. of pregnancy	Mode of delivery	Year of delivery	Gender	Blood group	Outcome
1st	Vaginal	2001	Female	Unknown	Still birth
2nd	Vaginal	2002	Male	Unknown	Permanent disability
3rd	Vaginal	2005	Male	Unknown	Neonatal death
4th	Vaginal	2008	Unknown	Unknown	IUD
5th	Vaginal	2011	Female	Unknown	Neonatal death
6th	LUCS	2014	Male	Unknown	Still birth

Her first five deliveries were by normal vaginal delivery and last one was done by C-section. Her anti-D titre was first done in our hospital on 29th October 2021 and found to be 1:32 (Figure 1). Her along with her husband's blood group was done in the year 2011 after her fifth pregnacy and her living son's blood group is yet to be known. She did not even receive anti-D immnoglobulin after any of her pregnacies ended.

No diagnostic or therapeutic measures were taken for this mother until now.

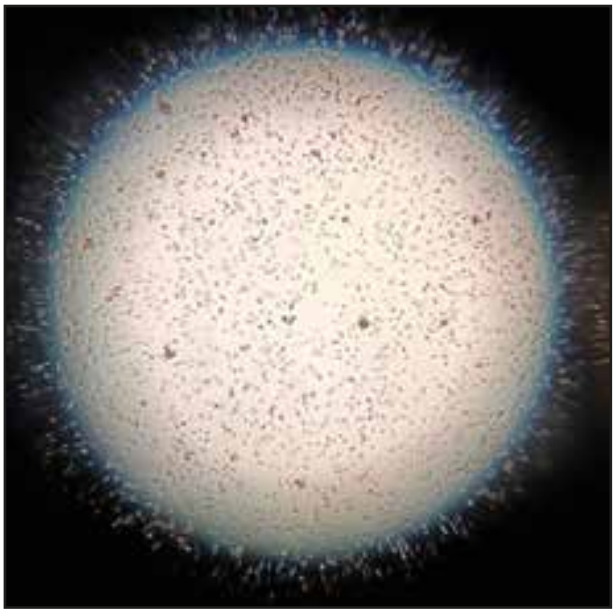

Figure 1: An anti-D titre of 1:32

Discussion

In humans, Rh antigenic determinants are inherited from each parent and direct the production of several blood group factors (C, c, D, d, E, e). Of these, Rh-D is the most important RBC antigen encountered in transfusion medicine, because it is the most immunogenic amongst all blood group antigens. In HDN due to Rh incompatibility, D antigen is responsible in about 90% cases. Rarely c, C and E antigens are implicated. The incidence of HDN due to D antigen is approximately thrice more common among Caucasians than blacks.[1,4]

Formation of anti-D antibody in Rh-D negative individuals is always secondary to exposure to Rh-positive RBCs. In females, this occurs either through mismatched blood transfusion, or more commonly, when Rh D-positive fetal RBCs enter maternal circulation during pregnancy, abortion or delivery. In the latter scenario, fetus inherits D antigen from its Rh D-positive father. Even 1ml of Rh D-positive red cells are enough to induce primary immune response.[1,5]

During pregnancy, the fetal and maternal circulations are separate. Red cells are not thought to cross the placental barrier in significant numbers in normal circumstances. Oxygen, nutrient and waste exchange takes place by diffusion across the intervillous space. IgG antibodies cross the placenta freely, carrying protection (passive immunity) for the fetus against infective agents to which the mother has had a healthy immune response.

Following delivery and placental separation, rupture of the placental villi and connective tissue allows escape of fetal blood cells into the maternal circulation, prior to constriction of the open maternal vessels. The incompatible Rh-D fetal cells enter the maternal spleen and the foreign antigen on the fetal red cell triggers off an immune response causing production of antibody.

In a subsequent pregnancy with an Rh D-positive fetus, the immune IgG anti-D maternal antibody will cross the placenta and attach to the specific D antigen sites on the fetal red cell. IgG-coated red cells do not have a normal lifespan. They are particularly sensitive to cells of the reticuloendothelial system and are removed from the circulation prematurely. Progressive anaemia in utero occurs from about the fourth month of pregnancy and, in the most severe cases, intrauterine death has been recorded from the 20th week of pregnancy, although it is uncommon before the 24th week.

Even though notable advances have taken place in the ability to determine fetal Rh-D status and in the prevention and management of fetal haemolytic disease, severe haemolytic disease still constitutes an interesting challenge.[6]

Antibody titers can be helpful in the evaluation of Rh immunized pregnancy.[7] In a classic study nearly four decades ago by Allen et al., 174 patients had antibody titers of 1:32 or lower, with no history of hydrops fetalis or stillbirth. Of these patients, 96% had live fetuses at 37 weeks' gestation.[7] In addition to anti-D titre, Kleihauer-Betke test or stainig should be done after a live birth to a Rh-D negative mother.

The other important manifestation of HDN is jaundice, often detectable from the first day of life. Due to rapid haemolysis, there is increase in fetal unconjugated bilirubin. In utero, it is cleared off by placenta and foetus remains essentially unaffect

ed. Following delivery, this protective mechanism is withdrawn causing a rapid surge in serum bilirubin. In untreated cases, the newborn's liver fails to conjugate this huge load and when serum level exceeds 340μmol/L (in term infants), unconjugated bilirubin gets deposited in brain leading to potential neurological damage (kernicterus).[4,8] However, reports exist in literature where only anaemia in the absence of jaundice has been the clinical presentation of Rh-HDN.4 Other potentially lethal co-morbidities of HDN that need clinicians' attention are hypoxia, acidosis and hypoglycaemia.[1,4,8]

With intensive plasmapheresis, maternal alloantibody can be reduced by as much as 75%. However, after 6–8 weeks, antibody levels tend to revert.[9] With this in mind, the aim of this treatment is mainly to help the fetus to pass the critical period until a definitive procedure could be performed. Plasma exchange permits the removal of antibody, immune complexes and may also have an effect on the immune system by enhancing the function of the reticuloendothelial system.[10]

Intrauterine fetal transfusion (IUT) is currently the therapy of choice in cases of severe anti-D isoimmunization presenting with fetal anemia. However, its efficacy is reduced in patients with early severe hydrops fetalis because of the technical difficulties in performing this procedure before 20 weeks' gestation.[11] In another study, it showed showed that immune globulin intravenous infusion (IVIG) delayed the onset of fetal anemia by 8–17 weeks, thus deferring the need for IUT.[12] However, some authors claim that high-dose IV gamma globulin does not seem to be useful in the treatment of severe Rh disease.[13]

In our patient, the significant anti-D titre of 1:32 along with the lack of proper procedures and treatment is hampering her to attain a successful pregnancy which in other words can be described as joy of life.

Conclusion

With this case, we would like to highlight the importance of blood grouping and Rh typing during the first antenatal visit and monitoring of red cell alloantibody development along with antibody titers, especially in a mother who is Rh-D negative. This is because the red blood cell alloantibody may lead to HDN of variable severity and this is preventable by timely anti-D immunoglobulin administration to all Rh-D negative mothers.

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