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Hemolytic disease of the newborn patient with rhesus incompatibility: a case report



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ABSTRACT

Introduction: Hemolytic Disease of the Newborn (HDN) is characterized by hemolytic anemia and jaundice. It arises when neonates' erythrocytes coated with sensitized antibodies are destroyed. Cases of HDN are still at high risk, particularly in women and children who are incompatible with rhesus. Reporting an instance of HDN with rhesus incompatibility was the goal of this investigation.

Case description: A 2-day-old male infant came with jaundice for less than 24 hours. Complaints are accompanied by dark urination. It is a second pregnancy, patient's mother routinely had her pregnancy checked by an obstetrician. The patient's mother was given rhesus immunoglobulin medication before giving birth and after giving birth. The patient was born with sectio caesarea, did not cry immediately, birth weight 2680 grams, 37 weeks with APGAR score 5-7. The first child is a still-alive boy with no similar complaints. The patient's mother has blood type O-, the patient's father (2nd husband) has blood type AB+, and the first child from her first husband has blood type O+. Laboratory test results support HDN with rhesus incompatibility, such as reticulocytosis, normochromic normocytic anemia, anisocytosis, hyperbilirubinemia, spherocyte and fragmentocyte in peripheral blood smear, the patient has blood type B+, crossmatch incompatible, coomb's test positive, examination of maternal rhesus antibody titer positive 1:512.

Conclusion: A 2-day-old male infant, HDN with rhesus incompatibility. Complaints, physical examination, and laboratory examinations confirmed the diagnosis. After 10 days of treatment, the patient was declared to have improved and was allowed to go home.

Keywords: hemolytic disease of the newborn, jaundice, rhesus incompatibility.

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INTRODUCTION

Baby erythrocytes coated with sensitized antibodies are destroyed, resulting in hemolytic anemia and jaundice, a condition known as Hemolytic Disease of the Newborn (HDN). According to estimates, there are 3-80 instances of hemolytic disease in the newborn for every 100,000 live births in the US each year. Rh antigen mismatch, also known as anti-D or anti-c, is highly uncommon in Asian women but affects 10% of pregnancies in White and Black women. About 15-25% of pregnancies are ABO incompatible, and 10% of those pregnancies result in HDN.¹⁻³

Alloimmunization involves exposing people without a particular blood group antigen to that antigen and having them produce corresponding antibodies. Exposure can come from receiving blood transfusions from donors or via unintentional fetal red blood cell transfer

into a pregnant woman's body, such as a fetal hemorrhage. When antibody production changes from the first IgM response to the IgG response, there will be an active transplacental transfer of maternal antibodies via neonatal Fc receptors. In the second and third trimesters, the transfer will happen faster and may result in HDN.⁴

Anemia in the pregnancy and newborn is the primary clinical symptom of HDN. Prenatal asphyxia, acute bilirubin encephalopathy, ascites, hydrops fetalis, congestive heart failure, intrauterine growth retardation, abdominal and pericardial edema, and kernicterus can all result from this. Exceeding the capacity of albumin-bilirubin binding, concentrations of unconjugated bilirubin can pass the blood-brain barrier and accumulate in the basal ganglia, ultimately resulting in the death of neurons. Hearing loss, cerebral palsy, mild neurodevelopmental

abnormalities, and even mortality can result from bilirubin encephalopathy, also known as kernicterus. Despite significant developments in HDN during the past 20 years, HDN cases remain a high risk, especially in mothers and children with rhesus incompatibility.⁵

CASE DESCRIPTION

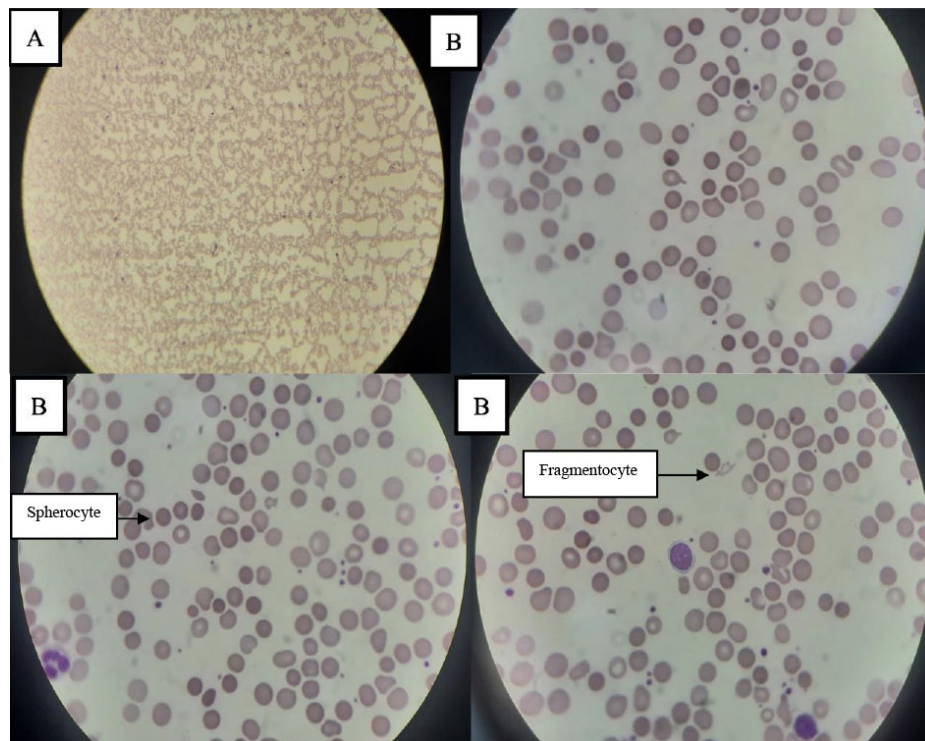
A 2-day-old male infant came with jaundice for less than 24 hours. Complaints are accompanied by dark urination. It is a second pregnancy, patient's mother routinely had her pregnancy checked by an obstetrician. The patient's mother was given rhesus immunoglobulin medication before giving birth and after giving birth. The patient was born with sectio caesarea, did not cry immediately, birth weight 2680 grams, 37 weeks with APGAR score 5-7. The first child is a still-alive boy with no similar complaints. The patient's mother

Table 1. Hematology results

	Units	Result	Reference
Reticulocytes	%	30.41	0.90-2.22
WBC	10 ³ /uL	18.78	9.10-34.00
Neutrophils		47.10	65.90-69.10
Lymphocytes		40.60	27.40-30.80
Monocytes		11.30	0-10.30
Eosinophils		0.60	0-5.80
Basophils		0.40	0-1.10
RBC	10 ⁶ /uL	1.90	4-6.60
HGB	g/dL	8.60	14.50-22.50
HCT	%	27.10	45-67
MCV	fL	142.60	92-121
MCH	Pg	45.30	31-37
MCHC	g/dL	31.70	29-36
RDW	%	29.10	14.90-18.70
PLT	10 ³ /uL	241	140-440
NLR		1.16	£3.13

Table 2. Clinical chemistry results

	Units	Result	Reference
Total bilirubin	mg/dL	20.60	<12
Direct bilirubin	mg/dL	1.25	0-0.5
Indirect bilirubin	mg/dL	19.35	0.2-0.7

**Figure 1.** Blood smear result. A. Objective magnification 10X, B. Objective magnification 100X.

has blood type O-, the patient's father (2nd husband) has blood type AB+, and the first child from her first husband has blood type O+.

Based on physical examination, the

patient had icterus (kremer V) and conjunctiva anemia. Laboratory test results support HDN with rhesus incompatibility. These results are also shown below (Table 1-2). As indicated by Table 1, a complete

blood count reveals an increase in reticulocyte and RDW and a reduction in hemoglobin and RBC. The clinical blood chemistry test results indicated an elevated bilirubin level, as shown in Table 2. The blood smear result concluded with normochromic normocytic anemia with spherocyte and fragmentocyte positive (Figure 1). The patient has blood type B+, and the patient's mother has blood type O-. Crossmatch results, major negative, minor, and auto control were positive. Both the Direct and Indirect Coomb tests yield promising findings. Maternal rhesus antibody titer analysis revealed a positive 1:512 result (Figure 2). Anamnesis, physical examination, and test findings led to the diagnosis of HDN with rhesus incompatibility in the patient.

DISCUSSION

The primary clinical manifestation of HDN is anemia in the fetus and neonate. It is observed as erythroblastosis fetalis.⁵ Jaundice is a condition that is often found in newborn babies. More than 50% of term newborns and 80% of preterm newborns experience icteric conditions. Jaundice experienced by neonates is classified as physiological jaundice and pathological jaundice. Jaundice that appears in the first 24 hours of life requires consideration of pathological jaundice, which can arise due to a significant increase in bilirubin, especially hemolysis due to ABO incompatibility or rhesus incompatibility and G6PD deficiency.⁶ The increased hemolysis causes hyperbilirubinemia, which will be seen initially on the face and spread caudally to the trunk and extremities. The examination results can be checked visually and quantified into grades 1 to 5 using the Kremer method.⁷

Hemolytic disorders that affect the fetus and newborn baby generally consist of two causes. First, congenital incompatibility between the mother's and fetus' blood types is known as ABO blood group incompatibility. Second, Fetomaternal Hemorrhage (FMH): the process of alloimmunization involves exposing people without a particular blood group antigen to that antigen and having them produce a specific antibody in response. Exposure can happen when a pregnant woman unintentionally absorbs

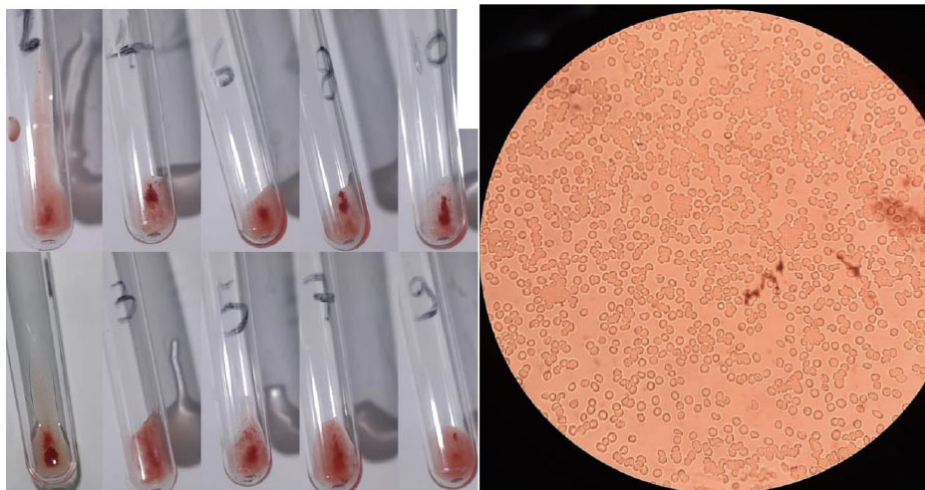


Figure 2. Results of maternal rhesus antibody titer examination with microscopic view.

fetal red blood cells, such as FMH. When antibody production changes from the first IgM response to the IgG response, there will be an active transplacental transfer of maternal antibodies via neonatal Fc receptors. In the second and third trimesters, this transfer will increase and may result in HDN illness.^{8,9}

The development of maternal antibodies following exposure to fetal blood is the mechanism in these people that causes HDN. Maternal antibodies may attach to antigens on the surface of fetal red blood cells as they enter the mother's bloodstream. The Rhesus D antigen is the most frequently seen in this mechanism. While severe anemia can result from this alloimmunization, most instances do not produce hemolytic illness in the baby.⁹

Reticulocytes are young, nucleated erythrocytes that retain RNA. The number of reticulocytes can increase due to acute bleeding and hemolytic anemia. There are various variations in the shape of erythrocytes. In the fragmentocyte cell form, the erythrocyte membrane is cut, and hemoglobin leaks through the membrane, causing anemia. In the form of spherocyte cells, they are rounder and thicker than normal erythrocytes. There is no pale part in the middle of the cell osmotically. They are more fragile than normal erythrocytes and can be found in the presence of a hemolytic process.¹⁰

At birth, the liver begins processing bilirubin. Indirect bilirubin is conjugated to direct bilirubin by the enzyme uridine diphosphoglucuronosyltransferase.

Direct bilirubin is excreted in bile, which will ultimately be excreted in feces and urine. The increase in bilirubin, in this case, is due to increased sequestration and hemolysis in red blood cells, causing ineffective clearance of fetal bilirubin from destroyed red blood cells.^{9,11}

In this patient, incompatible crossmatch results were obtained in minor and auto control. The crossmatch examination using the column agglutination test method, or the gel test, is carried out to ensure that there are no antibodies in the patient's serum that will react with the donor's blood cells if a transfusion is carried out. The degree of agglutination is assessed from 1+ to 4+ and the reaction is mixed-field for interpretation of crossmatch results. The erythrocytes on the surface of the gel are erythrocytes that have experienced agglutination. In contrast, the erythrocytes that have settled at the bottom of the gel have not experienced agglutination. Major crossmatch is a reaction between donor red blood cells and the patient's serum or plasma, while minor crossmatch is between the patient's red blood cells and donor plasma. The crossmatch results considered safe for the patient and that transfusion can occur are major, minor, and negative auto control. In this condition, the donor's blood is compatible with the patient's. If one or more crossmatch results are positive, the donor's blood is declared incompatible with the patient's blood. Incompatible crossmatch in this patient, the possible cause is due to the presence of maternal

rhesis autoantibodies on the baby's erythrocytes.¹¹

The antiglobulin test, also known as the Coombs test, is used to identify antibodies that attach to erythrocytes both in vitro and in vivo. The two Coombs test types are the Direct Coombs' (DCT) and Indirect Coombs' (ICT) tests. The former seeks to identify immune antibodies, including IgG and complement (usually C3d), that cover or sensitize red blood cells in vivo. In contrast, the latter seeks to identify incomplete complement or antibodies in the serum following an in vitro incubation with red blood cells.¹²

DCT examination is often used to help diagnose cases of HDN, AIHA, drug-induced hemolytic anemia, and transfusion reactions, while ICT is for instances of compatibility testing, screening, and identification of unexpected antibodies in serum and detecting red blood cell antigens using specific antibodies that only react with antiglobulins such as Fya, Fyb, JKa, Jkb, and others.¹²

Rhesus-negative mothers with rhesus-positive babies have a risk of the baby experiencing HDN because the mother experiences sensitization to form anti-D after being exposed to D antigen from fetal erythrocytes so that on examination, the mother's rhesus antibody titer is positive. These antibodies will enter the placental flow, causing the baby to experience hemolytic due to the binding of rhesus antibodies to the D antigen of infant erythrocytes. Checking the rhesus antibody titer is very helpful in determining what action to take. An increase in rhesus antibody titer twice or more excellent than 1:16 impacts the baby's condition significantly, and intensive perinatal care is recommended during pregnancy, labor, and the neonatal period.^{12,13}

The patient had phototherapy as part of their treatment for hyperbilirubinemia. For almost three decades, phototherapy has been the preferred treatment for jaundiced neonates since it has fewer side effects and works well. It is considered a first-line technique of treatment. Bilirubin undergoes photoisomerization to become water-soluble isomers that the kidneys and feces may eliminate without the liver having to handle them. The goal maximal exposure of the baby's body to light

irradiation in the blue-green wavelength range of 460–490 nm is one of the therapy modalities for hyperbilirubinemia.¹⁴ This study's limitation is that it did not report patient follow-up conditions, so it could not be evaluated in the longer term.

CONCLUSION

A 2-day-old male infant is diagnosed with HDN with rhesus incompatibility. The diagnosis was confirmed by complaints of jaundice since the baby was less than 24 hours old. Physical examination found anemia and jaundice. Laboratory examinations found a decrease in hemoglobin levels, reticulocytosis, peripheral blood smears found spherocytes and fragmentocytes, clinical chemistry test found increased bilirubin, examination of the patient's mother blood type O rhesus negative, the patient's blood type B rhesus positive, the Coombs test is positive, and the patient's mother rhesus antibody titer is positive. After 10 days of treatment, the patient was declared to have improved and was allowed to go home. Examination of blood rhesus should be done to avoid complications.

DISCLOSURES

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The authors declare no external funding for this study.

Conflict of Interest

The authors declare no conflict of interest.

Author Contribution

All authors equally contributed to the preparation of the article.

Ethical consideration

The patient's family has agreed regarding using cases in this case report.

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