

Haemolytic Disease of Newborn in a baby Delivered by Mother with Complete Anti-D Prophylaxis: An Unusual Case Report

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ABSTRACT

Haemolytic Disease of the Newborn (HDN), also known as erythroblastosis foetalis, is an immune-mediated disorder among neonates with a wide range of clinical presentations. The occurrence of HDN due to ABO-Rh incompatibility between the mother and baby is becoming rare due to increased knowledge of the disease and adherence to Good Clinical Practices (GCP) during pregnancy. This case report highlights a rare case of HDN in which, despite following GCP, standard care, an uneventful antenatal period, and timely administration of Anti-D immunoprophylaxis, the mother delivered a baby with HDN. The baby was successfully managed by a group of skilled and caring clinicians. Therefore, it is crucial to screen all at-risk mothers for HDN to identify it earlier and treat it successfully. This case report is rare in terms of the baby's survival with HDN born to a mother who had already received timely Anti-D immunoprophylaxis. Additionally, there is a need to emphasise on recent advances in diagnosis, such as foetal Doppler studies, and treatment options.

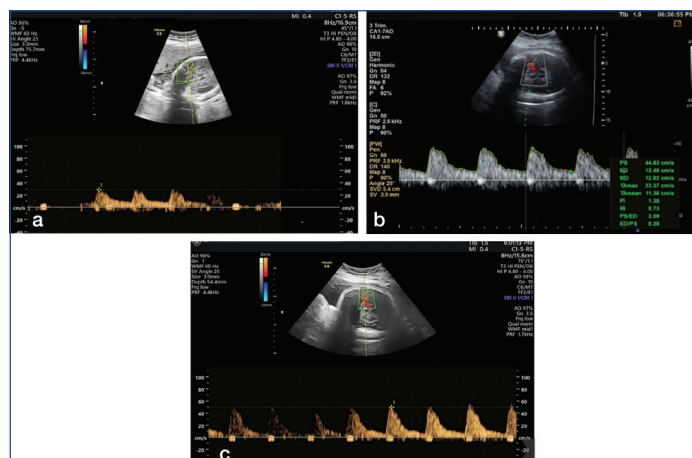
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CASE REPORT

A 34-year-old female, G2P2L1A0 with a blood group of A Rh negative, tested positive for the Indirect Coombs Test (ICT) during her second pregnancy at the 28th week of gestation. In her first pregnancy, she received 300 µg of Anti-D immunoprophylaxis at 28 weeks and immediately after a cesarean section via the intramuscular route. During her first pregnancy, the baby was born at 38 weeks of gestational age. The mother experienced mild pregnancy-induced hypertension, but the baby did not have any antenatal or postnatal complications.

During her second pregnancy with an uneventful antenatal period, she tested ICT positive with a titre of 1:64. Hence, the test was repeated immediately at another laboratory, which also confirmed the positive titre of 1:32, leading to the diagnosis of alloimmunisation.

Further evaluation was conducted under the guidance of a foetal medicine specialist who recommended regular foetal colour Doppler ultrasound focusing on Middle Cerebral Artery (MCA) Peak Systolic Velocity (PSV). Serial antenatal measurements of MCA-PSV were performed at 28, 33, and 35 weeks, respectively, and were within normal limits for gestational age [Table/Fig-1]. The eleven-cell panel tests for Anti-D Antibody showed positivity in five cell panels.



[Table/Fig-1]: Middle Cerebral Artery- Peak Systolic Velocity (MCA - PSV) presentation at a) 28 weeks; b) 33 weeks; c) 35 weeks.

The pregnancy was safely continued until 38 weeks of gestation under expert guidance. Delivery was carried out via LSCS to prevent uncontrolled Foeto-Maternal Haemorrhage (FMH) and hence placental transfer of alloantibodies. A baby boy weighing 3.2 kg with an APGAR score of 9 was born.

The neonatologist diagnosed mild HDN based on maternal history and haematological parameters [Table/Fig-2]. Thalassaemia was ruled out based on peripheral smear and Glucose-6-phosphate Dehydrogenase (G6PD) enzyme assay ruled out the deficiency of G6PD. Cord blood analysis excluded ABO incompatibility. On the second day, the baby was transferred to the Neonatal Intensive Care Unit (NICU) for 14 days due to a high total bilirubin

Parameter (Haemogram)	Result	Normal values
Haemoglobin (g/dL)	11.9	13.4-19.9
Haematocrit (%)	34.6	42-65
Red blood cell count (10 ⁶ /µL)	3.42	3.90-5.90
Mean Corpuscular Volume (MCV) (fL)	101.1	88-123
Mean Corpuscular Haemoglobin (MCH) (pg)	34.9	31-37
Mean Corpuscular Haemoglobin Concentration (MCHC) (g/dL)	34.5	28-36
Red cell Distribution Width (RDW) (%)	17.0	11.6-14.0
White blood cell count (10 ³ /µL)	24.1	9000-30000
Platelet count (10 ³ /µL)	450	150,000 to 450,000
Differential WBC count		
Neutrophils (%)	70.1	10.0-50.0
Lymphocytes (%)	16.9	40.0-67.0
Monocytes (%)	11.1	4.0-12.0
Eosinophils (%)	1.9	0.0-10.0
Basophils (%)	0.0	0.0-2.0
Peripheral blood smear		
RBC	Normocytic Normochromic. 1-2nRBC/100 WBC	
WBC	Leucocytosis	
Parasite	Not detected	

[Table/Fig-2]: Haematological parameters of day 2.

level of approximately 13.6 mg/dL and a low haemoglobin level of 11.9 g/dL.

Postnatal serial monitoring of haematological parameters and Liver Function Tests (LFT) was conducted for 14 days [Table/Fig-3]. Daily bilirubin levels were monitored, showing persistently high levels until the 9th day, followed by a decrease. Haemoglobin levels fluctuated from 11.9 g/dL on admission to as low as 8.6 g/dL at the time of discharge. A brain Ultrasonography (USG) was performed to rule out kernicterus.

Days	Hb gm/dL	PCV %	WBC μ L	Platelet μ L	Bilirubin		
					Total mg/dL	Conjugated mg/dL	Unconjugated mg/dL
Day 1	-----	-----	-----	-----	4.6	0.1	4.5
Day 2	11.9	34.6	24,000	450000	13.6	0.1	13.5
Day 3	9.4	27.4	14,000	380000	11.6	0.2	11.4
Day 4	9.1	26	16,000	410000	14.4	0.1	14.3
Day 5	7.6	20.8	12,200	410000	14.8	0.2	14.6
Day 6	12	33.7	4,800	490000	16.4	0.3	16.1
Day 7	11.4	32.3	23,200	480000	17.7	0.2	17.5
Day 8	-----	-----	-----	-----	17.2	0.9	16.3
Day 9	-----	-----	-----	-----	14.4	0.6	13.8
Day 10	-----	-----	-----	-----	10.5	0.2	10.3
Day 11	-----	-----	-----	-----	8.3	0.2	8.1
Day 12	-----	-----	-----	-----	8.8	0.2	8.6
Day 13	8.6	24.7	13,600	940000	10.1	0.1	10
Day 14	-----	-----	-----	-----	9.2	0.1	9.1
After 3 months	10.8	32.1	14000	600000	0.2	0.1	0.1

[Table/Fig-3]: Post natal Laboratory investigations of neonate diagnosed with HDN.

The treatment given to the newborn included intensive phototherapy for a total of 12 days, two days of Intravenous Immunoglobulin (IVIG), two Packed Cell Volume (PCV) transfusions, IV fluids, expressed maternal breast milk, and enteral folvite. Exchange transfusion was not considered as the baby responded well to the treatment provided. The baby was discharged successfully on day 15, being clinically stable, free from jaundice, although with low haemoglobin due to maternal antibodies circulation in the newborn's system for around three months, leading to haemolysis and anaemia.

The baby was followed-up until three months of age by a haematologist and neonatologist, treated with one PCV transfusion and a 5 mg dose of enteral folvite during this period, while maintaining normal LFT levels. Consent has been obtained from the parents to publish this case.

DISCUSSION

The HDN is a haemolytic condition that affects rhesus-positive infants born to rhesus-negative mothers. The incidence of HDN is estimated to affect around 3 to 8 out of every 100,000 patients per year [1]. The most common causes of HDN are ABO blood group incompatibility and FMH. The spectrum of HDN ranges from mild anaemia and insignificant hyperbilirubinemia to severe hydrops foetalis in newborns [2]. Although HDN impacts infants globally with a wide range of clinical symptoms, its prevalence in Asians is less than 1%, yet it remains concerning due to perinatal mortality and morbidity [1,3]. HDN was previously responsible for foetal loss in 1% of all pregnancies before the development of the Anti-D vaccine. Approximately 1 to 3 per thousand Rh-negative women develop alloimmunisation, even with proper RhD immunoprophylaxis. ABO mismatch affects 15 to 25% of pregnancies [1]. The spectrum of HDN varies from being asymptomatic to fatal and is classified as mild, moderate, or severe based on the levels of indirect bilirubin and haemoglobin. Treatment options vary accordingly and depend

on the gestational age of the baby, medical history, and the extent of the disease [2].

Recent advances in radiological diagnostic tools, such as measuring the MCA-PSV in the foetus, provide an effective, reliable, and non-invasive method for monitoring alloimmunised pregnancies at risk of foetal anaemia [2,4].

Treatment options during pregnancy include intrauterine blood transfusion based on serial USG Doppler examinations, the severity of anaemia, and the quantitative measurement of maternal anti-Rh

D antibodies. Postnatal treatment options include IV fluids, intense phototherapy, IVIG, and exchange transfusion for severe anaemia. Asymptomatic and undetectable FMH during pregnancy can expose Rh-negative mothers to Rh-positive red cells [2].

It is recommended that non-sensitised Rh-negative women delivering Rh-positive infants should receive Anti-D Ig (300 micrograms) IM or IV within 72 hours of delivery. Additional Anti-D can be administered if FMH exceeds 15 mL of foetal red blood cells [5]. Rhesus antibodies typically appear after the 28th week of pregnancy, significant transplacental haemorrhage may occur during pregnancy, and the half-life of Anti-D antibodies is approximately 17-22 days. Therefore, Anti-D should not be given before 28 weeks of pregnancy [6].

A similar case was described by Yousuf R et al., where a multiparous 30-year-old woman at 38 weeks of gestation, despite receiving anti-D prophylaxis at 28 weeks of gestation, delivered a full-term baby boy with HDN [7]. A systematic literature review of 60 articles on the antenatal landscape by de Winter DP et al., revealed a prevalence of 0.047% and 0.006% for Rh(D)- and K-mediated HDFN, respectively. The most frequently mentioned prenatal procedure was Intrauterine Transfusion (IUT). The range of the average gestational age at the first IUT was 25-27 weeks. There are dangers involved with this early time, which have been seen in IUT-related results. For pregnancies with Rh(D)-mediated HDFN treated with IUT, the rate of hydrops foetalis was 14.8% (range, 0-50%), but for K-mediated HDFN, it was 39.2%. The overall foetal death rate across 19 investigations was 19.8%±29.4%, with a mean±SD. The range of the mean gestational age at birth was 34 to 36 weeks [8].

Of the 29,663 pregnant women tested at the Department of Transfusion Medicine by Raguz MJ et al., 545 (1.8%) had antibodies against antigens detected by the Indirect Antiglobulin Test (IAT). Over the course of a 20-year trial in West Herzegovina, 310 (1.0%) newborns with HDN received treatment. According to the study findings, 230 out of 545 pregnant women, or 42%, had received the ABO vaccination. 64% (199/310) of newborn infants with HDN

had ABO HDN, which is the most frequent type. Only 19% (59/310) of newborns with RhD HDN received treatment. The lack of non-RhD immunisation preventative programs and the inconsistent immunological screening of RhD-positive pregnant women in the area were the causes [9].

Despite timely maternal Anti-D prophylaxis, the probability of HDN development in offspring in this case may be due to an inadequate dose of Anti-D that was disproportionate to FMH or the potency of the Anti-D injection.

The case under discussion involved mild HDN, which was promptly diagnosed and carefully monitored by a team of dedicated medical professionals. Consequently, the pregnancy continued for 38 weeks without any apparent advancement of HDN, and additional complications associated with preterm birth were averted.

CONCLUSION(S)

This case report is unusual in terms of the survival of a baby with HDN born to a mother who had already received timely Anti-D immunoprophylaxis. Additionally, ICT must be performed during pregnancy regardless of Anti-D prophylaxis. Despite timely Anti-D prophylaxis, alloimmunisation and HDN can occur, as in this case. Recent advancements in radiological diagnostic tools, such as measuring the MCA-PSV in the foetus, provide an effective, reliable, and non invasive approach to monitoring alloimmunised pregnancies at risk of foetal anaemia. HDN is preventable and not always fatal.

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