

Case Report

Protracted haemolytic disease of newborn due to Rhesus isoimmunisation by passive acquisition of anti-D antibodies through breast milk

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Background

Rhesus isoimmunisation is a well-recognised cause of haemolytic disease of the newborn (HDN), which could lead to severe haemolysis within the first few days of life. It typically presents in the first 48 hours of life, and the haemolysis is complete by 14 days. It is caused by the placental transfer of Rhesus anti-D antibodies from a sensitised mother to her offspring. Passage of Rhesus anti-D antibodies in human breast milk causing haemolysis in the baby is very rare. Here, we report a 23-day-old neonate with prolonged haemolysis due to acquisition of Rhesus anti-D antibodies through maternal breast milk, causing persistent haemolysis, anaemia and hyperbilirubinemia.

Case presentation

A thirty-year-old AB-negative woman gave birth to a neonate at 33 weeks of gestation. She had a triplet miscarriage at 19 weeks of gestation in the past, following which a single dose of RhoGAM was given. During the current pregnancy, her Rhesus anti-D antibodies were positive at the booking visit, and the baby was delivered via emergency lower segment caesarean section due to rising antibody titres (1:520) and fetal anaemia detected in Doppler studies.

The baby did not cry at birth and required resuscitation with one cycle of inflation

breaths. APGAR scores at 1 and 5 minutes were 6 and 9 respectively, and the birth weight was 2145g. He developed mild respiratory distress soon after birth and managed for mild surfactant deficient lung disease with nasal continuous positive airway pressure.

The cord blood total bilirubin was 68µmol/L with indirect bilirubin of 55µmol/L (phototherapy range 40-80µmol/L) and haemoglobin was 15.6g/dL. The baby's blood group was A positive, and the direct antiglobulin test (DAT) was highly positive (IgG 4+ and C3d negative). The blood picture showed evidence of haemolysis. HDN due to Rhesus isoimmunisation was diagnosed, and the baby was started on double-surface phototherapy soon after birth and given intravenous immunoglobulin 1g/kg on day one of life. He received phototherapy from day one to four and was discharged home on day five on exclusive breastfeeding when bilirubin was well below the phototherapy level. He was followed up until the 14th day of life and he remained to have normal serum bilirubin levels.

He presented again with jaundice and a total bilirubin of 264µmol/L (indirect bilirubin 244µmol/L) on the 23rd day of life. His full blood count revealed haemoglobin- 8.6g/dL,

white cell count- $9.6 \times 10^9/L$, and platelet count- $314 \times 10^9/L$.

Biochemical investigations revealed aspartate transaminase-13IU/L, alanine transaminase- 9IU/L, and C-reactive protein $<5\text{mg/L}$. The blood picture showed normochromic normocytic red blood cells (RBCs), polychromatic cells, and occasional nucleated RBCs, indicating ongoing haemolysis. His reticulocyte count was 6% (normal 1-2%), and DAT remained highly positive (IgG 3+). Further evaluation revealed strong positivity of anti-D in maternal breast milk, indicating passage of Rhesus anti-D antibodies through breast milk to the baby.

Prolonged HDN due to Rhesus isoimmunisation by the passive acquisition of anti-D antibodies through maternal breast milk was diagnosed. The baby was given a second dose of intravenous immunoglobulin 1g/kg and a 10mL/kg packed RBC transfusion. The post-transfusion haemoglobin was 12.6g/dL. Transient cessation of breastfeeding was attempted; however, it failed due to the development of cow's milk intolerance. The baby responded well to intravenous immunoglobulin and jaundice, and serum bilirubin gradually declined. At six weeks, his haemoglobin was 10.4g/dL, bilirubin was $75\mu\text{mol/L}$, and his blood picture did not show evidence of haemolysis. Breast milk became negative for Rhesus anti-D antibodies, and repeat DAT was negative.

Discussion

HDN is caused by antibodies formed against over 50 RBC antigens; however, it is most commonly caused by antibodies formed against Rhesus antigens¹. Of the Rhesus antibodies, Rhesus anti-D is the most commonly reported cause of HDN. In addition to Rhesus antibodies, HDN is caused by the incompatibility of the ABO blood group. Less common causes of HDN include antibodies directed against antigens of the Kell blood group (e.g., anti-K and

anti-k), Kidd blood group (e.g., anti-Jka and anti-Jkb), Duffy blood group (e.g., anti-Fya), and MNS blood group².

HDN of Rhesus isoimmunisation is characteristically caused by the transplacental passage of maternal IgG antibodies to the fetus in utero. Hence, it typically presents within the first 48 hours of life, and the severity gradually weans off with time. This case report presents a neonate with worsening jaundice and hyperbilirubinemia during the fourth week of life. Ongoing haemolysis was evident by reticulocytosis, polychromatic cells in the blood picture, and persistently positive DAT. This prompted us to examine the sources of the continuing passage of anti-D antibodies, which confirmed the passage of anti-D via maternal breast milk.

A few previous studies had shown the presence of anti-D antibodies in breast milk leading to ongoing haemolysis in Rhesus-positive babies born to Rhesus-negative mothers^{1,3,4}. Similarly, there are reports of persistent neonatal thrombocytopenia caused by antiplatelet antibodies of immune thrombocytopenia mothers transmitted through breast milk⁵. In both instances, the cessation of breastfeeding had been a successful mode of treatment^{3,5}. However, in our patient, we could not stop breastfeeding due to the development of cow's milk protein intolerance; hence, the baby continued to have breast milk. We treated the child with intravenous immunoglobulin, to which the child responded.

In conclusion, this case report presents a very rare instance of prolonged haemolytic disease of newborn due to Rhesus isoimmunisation by passive acquisition of anti-D antibodies through maternal breast milk. It also highlights the successful treatment with intravenous immunoglobulin when discontinuing breastfeeding is not feasible.

References

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