Anti-S antibodies: an unusual cause of haemolytic disease of the fetus and newborn (HDFN)

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SUMMARY

We report a case of haemolytic disease of the fetus and newborn due to anti-S antibodies. Baby G was born by emergency caesarean section at 35 weeks due to reduced fetal movement. Prior to delivery, antenatal screening revealed the mother's blood group was AB rhesus positive with anti-S antibody titres. The baby was pale but non-hydrotic at birth with hepatosplenomegaly. Haemoglobin at birth was 5.23 g/dl and serum bilirubin 138 µmol/l. The baby required phototherapy, γ-globulin infusion and exchange transfusion with post-transfusion complications.

BACKGROUND

Haemolytic disease of the fetus and newborn (HDFN) resulting from maternal immunoglobulin G antibodies (alloimmunisation) crossing the placenta into fetal circulation during pregnancy causes HDF in utero and HDN after delivery.

More than 43 different red cell antigens have been reported to be associated with HDFN.¹ In a 2-year study (1993–1995) in New York serum samples from 37 506 were evaluated and a positive screen for antibodies known to be associated with HDFN in 424 (1.1%) of the samples.² Rhesus antibodies accounted for over half of the positive screens (55.9%), Kell (28.5%), Duffy (7.1%), MNS (5.7%), Kidd (1.9%), Lutheran (0.7%) and others (0.2%). Historically, however, the incidence of rhesus alloimmunisation has declined from 14% to 1–2% following the introduction of rhesus immunoglobulin (RHIG) in the 1960s to 0.1% after 1979 with the addition of routine antenatal RHIG prophylaxis.³ Recently, other antibodies have surpassed anti-D in some studies as causes of alloimmunisation. In a large study in the Netherlands, of 1133 Dutch women with a positive antibody screen, anti-E was the most commonly detected (23%) followed by anti-K (18.8%), anti-D (18.7%) and anti-C (10.4%).⁴

However, not all antibodies are associated with severe HDFN. Severe haemolytic disease requiring intrauterine transfusion (IUT) was caused by anti-RhD (85%), anti-Kell (10%) and anti-RhC (3.5%) in a 2005 Dutch study.⁵ Overall results from another 2008 Dutch study showed severe HDFN requiring IUT or exchange transfusion in 3.7% at risk fetuses; with 11.6% in anti-K, 8.5% in anti-C, 1.1% in anti-E, 3.8% in Rh-antibodies other than anti-C, anti-D or anti-E and none in other antibodies other than Rhesus and Kell.⁶

CASE PRESENTATION

A girl, Baby G, was born at 35 weeks+2 days, by emergency caesarean section for reduced fetal

movement to a 38-year-old G4P3+0 Irish Caucasian mother. At antenatal booking in the first trimester, mother's blood group was AB Rh+ with a positive antibody screen for phenotype big S. Her initial anti-S indirect antiglobulin titre was 1:64, her other prenatal screen for HIV, Venereal Disease Research Laboratory and hepatitis were all negative and she was rubella immune. She had three previous full term normal deliveries. Her third child was diagnosed with mild direct coombs test (DCT) positive jaundice with serum bilirubin (SBR) levels below phototherapy range.

The mother had a routine antenatal period during which she was informed of the presence of anti-S antibodies and referred appropriately to a tertiary fetomaternal specialist. On the day of delivery, the mother presented to her local hospital at a gestational age of 35 weeks+2 days with decreased fetal movement which was confirmed on fetal monitoring. Two hours after presentation, an emergency caesarean section was carried out and a live girl was delivered. The baby cried at delivery and required no resuscitation. The baby was given APGAR scores of 9 at 1 min and 9 at 5 min.

General physical examination showed a pale, non-hydrotic, anicteric infant with a birth weight of 2750 g. Systemic examination showed normal cardiovascular and respiratory status. The infant, however, had clinically significant hepatosplenomegaly (liver 5 cm and spleen 6–7 cm below costal margins). Cord bloods were taken for full blood count (FBC), SBR, blood group and DCT (figure 1).

TREATMENT

On admission to the neonatal unit initial vitals showed heart rate 151/min, respiratory rate 52/min, temperature 36.6°C and SaO₂ of 90%. The baby was placed in an incubator and an intravenous cannula was sited and repeat samples for FBC, SBR and blood culture obtained. Blood results from cord blood showed haemoglobin (Hb) 5.23 g/dl, haematocrit (HCT) 16.5, white cell count 20.1, platelets 90.6, SBR 138 µmol/l, AB Rh– blood group and DCT positive result.

Intravenous antibiotics, benzylpenicillin and gentamicin were started and supplemental oxygen was supplied via the incubator as SaO₂ was only 90% and there was dyspnoea with mild subcostal recessions. The baby was kept nil per oral and started on intravenous fluid 10% dextrose at 60 ml/kg/day. Phototherapy was also started immediately with a phototherapy blanket and three overhead lights. Repeat sampling for FBC and SBR at 1 h of life showed consistently marked anaemia, Hb 6.13 g/dl and Hct 20 with increasing levels of unconjugated bilirubin, 164 µmol/l. A TORCH screen for

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Figure 1 Illustration of the changes in measured serum bilirubin which peaks in the first four hours immediately prior to the infant's double-volume exchange transfusion. As expected there was a postexchange transfusion rebound which was managed conservatively with phototherapy.

parvovirus, toxoplasma, cytomegalovirus, hepatitis and rubella was also obtained. Umbilical arterial and venous lines were placed (figure 2).

Location of the hospital 2 h away from the centralised blood bank services created a logistics problem but decision to stay in the local hospital and not transfer to a tertiary institution was taken in consultation with local consultant staff, tertiary hospital consultants and parents. In the interim the baby received two doses of 1 g/kg (total dose 2 g/kg) of intravenous γ -globulin.

The baby had a double volume exchange blood transfusion completed 8 h post delivery. The procedure was clinically well tolerated. However, on post-transfusion, the baby developed hypocalcaemia, despite intraexchange calcium gluconate replacement and dilutional thrombocytopenia necessitating calcium infusion and platelet transfusion (10 ml/kg), respectively. The baby was started on oral feed on day 3 of life, received 5 days of intravenous antibiotics, 6 days of phototherapy and spent a total of 14 days in the neonatal unit. Prior to discharge, the baby was on full feeds orally with Hb and SBR in the normal range and hepatosplenomegaly had also resolved. Outpatient appointments for audiology assessment and paediatric review clinic were planned for post-discharge follow-up. The infant's

Figure 2 Repeat sampling for haemoglobin and haematocrit while an inpatient and following discharge illustrate severe anaemia at birth, improvement postexchange transfusion and gradual deterioration during follow-up.

clinical assessment, including her neurological examination, was normal at discharge.

OUTCOME AND FOLLOW-UP

Follow-up in the outpatient department (OPD) continued to show a neurologically normal and thriving child; however, blood sampling in the OPD showed an evolving late anaemia, the baby was started on iron supplements.

DISCUSSION

Anti-S antibodies are usually produced after red cell sensitisation in an S antigen negative mother with S antigen positive fetus. It is capable of producing HDFN usually of mild variance.

In one series of 175 000 pregnancies in the Oxford region of England, anti-S antibody was detected in 22 pregnancies in 19 women.⁷ Previous blood transfusions were thought to be the cause of sensitisation in 13 women. Only four tested DCT positive and only one infant required exchange transfusion.

Only a few cases of severe HDFN associated with anti-S have been described in the literature. The first in 1952 reported by Levine *et al*⁸ resulted in early infant death due to kernicterus; Griffith⁹ reported a case of stillbirth at 41 weeks gestation with positive maternal anti-S antibody and autopsy findings in keeping with fetal hydrops.¹⁰ Finally, Mayne *et al*⁷ reported a case of maternal anti-S alloimmunisation resulting in the birth of an infant requiring three exchange transfusions and 5 days of phototherapy.

Learning points

- ▶ Anti-S alloimmunisation is usually a cause of mild haemolytic disease of the fetus and newborn (HDFN); however, we report a case of HDFN resulting in severe HDFN, a relatively rare presentation.
- ▶ Severe alloimmunisation is a cause of significant morbidity and mortality, the management is multidisciplinary with significant recourse to hospital resources.
- ▶ Definitive management with exchange transfusion is usually required for severe HDFN, complications of treatment, in this case, hypocalcaemia and thrombocytopenia could be significant.
- ▶ Follow-up care with emphasis on the neurodevelopmental outcome, hearing and late onset anaemia should be evaluated.

Competing interests None.

Patient consent Obtained.

REFERENCES

- 1 Weinstein L. Irregular antibodies causing haemolytic disease of the newborn: a continuing problem. *Clin Obstet Gynecol* 1982;25:321–32.
- 2 Geifman-Holtzman O, Wojtowycz M, Kosmas E, *et al*. Female alloimmunization with antibodies known to cause haemolytic disease. *Obstet Gynecol* 1997;89:272–5.
- 3 Eder AF, Manno CS. Alloimmune haemolytic disease of the fetus and newborn. In: Greer JP, Foerster J, Lukens JN, *et al*, eds. *Wintröbe's clinical hematology*. 11th edn. Philadelphia, PA: Lippincott, Williams & Wilkins, 2004.
- 4 Van der Schoot CE, Tax GH, Rijnders RJ, *et al*. Prenatal typing of Rh and Kell blood group systems antigens: the edge of a watershed. *Med Rev* 2003;17:31–44.
- 5 van Kamp IL, Klumper FJ, Oepkes D, *et al*. Complications of intrauterine intravascular transfusion for fetal anemia due to maternal red cell alloimmunization. *Am J Obstet Gynecol* 2005;192:171–7.

- 6 Koelewijn JM, Vrijkotte TGM, van der Schoot CE, *et al*. Effect of screening for red cell antibodies, other than anti-D, to detect haemolytic disease of the foetus and newborn: a population study in the Netherlands. *Transfusion* 2008;48:941–52.
- 7 Mayne KM, Bowell PJ, Green SJ, *et al*. The significance of anti-S sensitisation in pregnancy. *Clin Lab Haematol* 1990;12:105–7.
- 8 Levine P, Ferraro LR, Koch E. Hemolytic disease of the newborn due to anti-S. *J Pediatr* 1973;82:88–91.
- 9 Griffith TK. The irregular antibodies: a continuing problem. *Am J Obstet Gynecol* 1980;137:174–7.
- 10 Vengelen-Tyler V. *Technical manual of the American association of Blood Banks*. 1999. Bethesda, MD: America.

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