Paediatrics & Child Health, 2017, 238–239
doi: 10.1093/pch/pxx076
CPSP Highlights
Advance Access publication 31 May 2017

CPSP Highlights

Rh sensitization in Canada is not obsolete

Jillian M. Baker MD MSc FRCPC[1,2], Douglas M. Campbell MD MSc FRCPC[1], Vinod K. Bhutani MD FAAP[3], Michael Sgro MD FRCPC[1]

[1]Department of Pediatrics, St. Michael's Hospital, Toronto, Ontario; [2]Division of Haematology-Oncology, The Hospital for Sick Children, Toronto, Ontario; [3]Department of Pediatrics, Lucille Salter Packard Children's Hospital, Stanford Children's Health, Stanford University, Stanford, CA, USA

Correspondence: Jillian M. Baker, Department of Pediatrics, St Michael's Hospital, Pediatrics Clinic 2nd Floor, 61 Queen St. East Toronto, Ontario M5C2T2. e-mail bakerji@smh.ca

Neonatal-Perinatal Medicine; Hematology; Maternal-Fetal Medicine.

Keywords: *Hemolytic disease of the newborn*; *Hyperbilirubinemia*; *rhesus isoimmunization*.

CASE

A 35-year-old G3P1TA1 female, blood type A-negative was found to have anti-D antibodies during her previous pregnancy, and that infant required intensive phototherapy for jaundice.

Early in her current pregnancy, high-titre anti-D antibodies were detected. However, unexpectedly, fetal transfusion was not required. This infant was born at 36 weeks gestation by induced vaginal delivery for fetal anemia and was clinically well. The infant's blood type was A-positive and the direct antibody (DAT) on the cord blood was positive with maternal anti-D on the infant's red blood cells (RBCs).

The infant's indirect bilirubin was 165 μmol/L at 6 hours of life and climbed steadily (rate of rise 5 μmol/L/hour) during the first few days of life despite anticipatory intensive phototherapy. The hemoglobin on the cord blood complete blood count (CBC) was slightly low at 130 g/L. On day 2 and 3 of life, intravenous immunoglobulin (IVIG) was administered (1 g/kg/dose) in an effort to avoid the need for exchange transfusion (1,2). The hemoglobin fell slowly over the course of the first 3 days of life and the infant was transfused packed RBC twice in the first week of life.

It was unclear how this woman became sensitized to D antigen. Her first pregnancy ended in a therapeutic abortion, with no maternal RBC antibodies detected, and she received prophylactic Rh immunoglobulin (RhIg) before the procedure. She was sensitized to D antigen at the time of routine antenatal screening at the beginning of her second known pregnancy. Upon further questioning, she recalled an extremely heavy, late menstrual period between her abortion and her next known pregnancy. This history is in keeping with an early unrecognized spontaneous abortion with a missed opportunity for primary prevention, resulting in D-antigen sensitization.

LEARNING POINTS

- Rhesus (Rh) hemolytic disease is the result of maternal–fetal Rh(D)-antigen incompatibility, and refers to the sequelae associated with maternal sensitization. Rh sensitization occurs when women whose red blood cells are Rh(D)-antigen negative develop anti-Rh(D) antibodies either during a previous pregnancy in which the fetus is Rh(D)-positive or by exposure to Rh antigens from blood products/transfusion. Progressive anemia and hydrops fetalis resulting in stillbirth or early neonatal death are possible consequences of severe hemolytic disease in utero. Neonates may present with severe jaundice, anemia and death from acute or chronic bilirubin encephalopathy.
- Rh disease was once the most common and most severe cause of fetal and neonatal hemolysis until the implementation of postpartum Rh immunoglobulin prophylaxis. This has been a highly effective public health measure for the prevention of neonatal morbidity and mortality. Whereas Rh-disease was first recognized in 1609, the Rh system was established in 1940, causation was attributed in 1950 and the WHO recommended immune prophylaxis in the 1970s.
- Prenatal Rh screening is now a routine part of prenatal and obstetrical care in most developed countries, as is prophylaxis with Rh immunoglobulin for Rh(D)-antigen-negative mothers. As such, Rh disease is now rare outside of South Asia, sub-Saharan Africa and Eastern Europe where an estimated 373,300 cases occur annually (3). However, several factors may lead to cases in Canada such as missed opportunities for prevention (as described in our case), or immigration and refugees from diverse countries that could result in the potential influx of mothers into Canada who have not received adequate health education or Rh prophylaxis with previous pregnancies and procedures. The current incidence of maternal Rh(D)-negative status, sensitization and Rh disease-associated neonatal severe hyperbilirubinemia in Canada is unknown.
- The majority of the complications of Rh hemolytic disease of the newborn can be managed with prenatal interventions including the use of Rh immunoprophylaxis, surveillance for fetal anemia, early signs of cardiac failure and hydrops, and if needed, the timely use of intrauterine transfusion.
- Rh-negative women need extensive and repeated prenatal and postpartum counselling regarding the risk of Rh sensitization during known pregnancies, possible pregnancies and miscarriages. They also should be advised to remind health care workers about their Rh status prior to elective and emergency surgeries that may carry a risk of red cell transfusion, and be advised that sensitization can occur with contaminated needle sharing.
- A number of risk factors have been found to be associated with severe hyperbilirubinemia in the newborn including jaundice visible before discharge from hospital (especially if evident in the first 24 hours of life), previous sibling with jaundice, Asian race, gestational age between 35 and 37 weeks,

inadequate exclusive breast feeding, male gender and infant bruising/cephalohematoma. Additional risk factors identified by laboratory investigations include ABO incompatibility (regardless of DAT result), glucose-6-phosphate dehydrogenase (G6PD) deficiency and Rh sensitization and rare causes of inherited red blood cell disorders (4).

- Through our CPSP survey, Canadian paediatricians will be asked to report any infant 60 days of age or less with Rh (D) sensitization fulfilling ALL of the following criteria: (1) Mother is Rh-negative (D-negative); (2) Mother has a positive antibody screen due to anti-D (This must be a maternal allo-anti-D, not passive anti-D from Rh immunoglobulin [RhIg]); (3) Cord or infant blood group is Rh-positive (D-positive).
- The objectives of our CPSP surveillance study are to estimate the incidence of maternal Rh sensitization in Canada, and the incidence of Rh disease-associated neonatal severe hyperbilirubinemia in Canada. Additionally, we aim to identify the timing of presentation, etiology and associated triggers or risk factors for Rh sensitization and Rh disease-associated neonatal severe hyperbilirubinemia in Canada such as immigration patterns, Rh immunoglobulin (RhIg) refusal and Rh sensitization prior to 28 weeks gestation.

References

1. Alcock GS, Liley H. "Immunoglobulin infusion for isoimmune haemolytic jaundice in neonates." Cochrane Database Syst Rev 2002;(3):CD003313.
2. Barrington KJ, Sankaran K. Canadian Paediatric Society Fetus and Newborn Committee. "Guidelines for detection, management and prevention of hyperbilirubinemia in term and late preterm newborn infants." Paediatr Child Health 2007;12(Suppl B):1B–12B.
3. Bhutani VK, Zipursky A, Blencowe H et al. Neonatal hyperbilirubinemia and rhesus disease of the newborn: Incidence and impairment estimates for 2010 at regional and global levels. Pediatr Res 2013;74 Suppl 1:86–100.
4. Sgro M, Campbell D, Shah V. Incidence and causes of severe neonatal hyperbilirubinemia in canada. CMAJ 2006;175:587–90.