Case Report

Rhesus haemolytic disease of the newborn, complicating a quadruplet pregnancy

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Quadruplet pregnancy is extremely rare, although the incidence has risen since the late 1970s due to the increased use of infertility treatment. The occurrence of spontaneous quadruplet pregnancy is estimated to be one in 571,000 births using Hellin’s hypothesis.1

Rhesus haemolytic disease of the newborn (Rh.HDN) occurring in multiple pregnancy is also a rare event but it has been reported in twins2,3 and in a triplet pregnancy.4 In this paper we report a spontaneous quadruplet pregnancy complicated by severe Rh.HDN.

Case Report A 26 year old Caucasian woman received an anti-D immunoglobulin after the delivery of her first child who was born at 41 weeks’ gestation by normal vaginal delivery in 1991. There was no history of blood transfusion, abortion or stillbirth between the first and second pregnancy.

She was booked at about five weeks’ gestation in a small general hospital and transferred to Royal Maternity Hospital, Belfast, at 24 weeks’ gestation when quadruplet pregnancy was confirmed. She remained in hospital for six weeks and four days until delivery. There was no past medical history of note, blood group was O-Rh(D) negative and anti-D antibodies were detected (Table). The husband’s blood group was O-Rh(D) positive and his probable genotype was CDe/cDE.

The status of the mother and fetuses was closely monitored and assessed in hospital by Doppler studies, cardiotocography and regular ultrasound scanning. Amniocentesis was performed on three occasions.

The results of amniocentesis and lecithin/sphingomyelin area ratio are shown in the Table. She was given five courses of betamethasone 12 mg intramuscularly twice a week until she went into spontaneous labour at 30 weeks and four days of gestation. An emergency Caesarean section was performed under general anaesthesia. Placental pathology was unremarkable and there were no retroplacental or marginal clots.

QUADRUPLET I
The first baby was a boy, weighing 1124 g with Apgar scores of 7 and 8 at one and five minutes respectively and he had no signs of respiratory distress or hydrops.

Cord haemoglobin was 7.3 g/dl, cord bilirubin was 87 umol/L, blood group (Bl.gp) was O Rh(D) positive and direct Coombs test (DCT) positive. He was initially given a ‘top up’ blood transfusion of packed red cells and phototherapy for eight days. He required five exchange blood transfusions for hyperbilirubinaemia. He was also given two units of platelets for post-exchange thrombocytopenia.

QUADRUPLET II
The second baby was a boy weighing 1307 g with Apgar scores of 8 and 8 at one and five minutes respectively. There were no signs of hydrops. However in the first hour of life he developed mild respiratory distress which settled with brief...
facial oxygen therapy. His cord haemoglobin was 8.3 g/dl, cord bilirubin was 71 umol/L, Bl.gp was O Rh(D) positive and DCT positive. He had six days of phototherapy, a 'top up' of packed red cells and two exchange transfusions.

QUADRUPLET III

The third baby was a girl with Apgar scores of 5 and 7 at one and five minutes respectively, her birth weight was 796 g and she had no signs of hydrops.

Cord haemoglobin was 10.9 g/dl, cord bilirubin was 79 umol/L, Bl.gp was O Rh(D) positive and DCT positive. She also was given a 'top up' of packed red cells, phototherapy for seven days and two exchange transfusions were required.

QUADRUPLET IV

A girl with Apgar scores of 5 and 7 at one and five minutes respectively, her birth weight was 892 g. Her cord haemoglobin was 10.7 g/dl, cord bilirubin was 72 umol/L, Bl.gp was O Rh(D) positive and DCT positive. She had recurrent apnoeic spells at the age of two hours requiring ventilatory support for 24 hours. She also required a 'top up' blood transfusion and phototherapy for seven days; and three exchange transfusions were given.

Milk feeds were commenced on day five for quadruplet I, II and III and on day six for quadruplet IV, and went up uneventfully, allowing quadruplet I and II to be discharged home aged five weeks weighing 1775 g and 1993 g respectively, whereas Quadruplet III and IV were discharged on day 45 of life weighing 1656 g and 1776 g respectively.

DISCUSSION

The number of babies affected with Rh.HDN has decreased since the introduction of anti-D immunoglobulin prophylaxis in 1969. 3 There has been a similar decline in the number of deaths of affected babies. 6 This trend has been mainly attributed to improved obstetric and neonatal care especially in developed countries.

In the quadruplet pregnancy we describe, regular ultrasound studies showed no evidence of hydrops but revealed a pattern of intrauterine growth retardation in quadruplet III and IV. Amniocentesis was performed on quadruplet II who was used as a control by mapping of the membranes guided by ultrasound. The amniobilirubin results presented in the Table showed an overall reduction in the optical density values at 450 NM from midzone-II to lower zone-II plotted on Liley’s graph, 7 so that an intrauterine transfusion was not indicated.

Amniocentesis was not a particularly helpful tool in predicting the severity and outcome of Rh.HDN in this case. The father was homozygous for D-antigen at Rh. locus, so all the babies were Rh.D positive. Maternal anti-D antibody titres had increased steadily during this pregnancy making it possible that the mere presence of quadruplets in themselves and the large surface area of combined placentas had caused a more severe rhesus sensitisation than one might expect with a second pregnancy in this patient. There was no ABO blood group incompatibility between the mother and the fetuses.
A previous study showed that ABO incompatibility could account for the difference in severity of Rh.HDN between twins. Other studies however have failed to show this, and have postulated that other factors such as differences in placental perfusion, fetal erythropoiesis and fetal hepatocellular function may be responsible for the disparity in severity of Rh.HDN between individual fetuses in multiple pregnancies.

Our case also shows that the standard anti-D prophylaxis dose is not protective in higher multiple pregnancies.

It took sixteen hours to perform all the exchange transfusions and collectively they required 17 days of ‘level one’, 46 days of ‘level two’ and 98 days of ‘level three’ care (see reference 8).

In spite of the decreasing incidence and severity of Rh.HDN, it still imposes a considerable degree of morbidity in some babies, demanding highly skilful antenatal and neonatal care particularly in multiple pregnancy. From a review of the literature, this report is the first of Rh.HDN affecting a spontaneous quadruplet pregnancy.

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