Prenatal treatment of fetomaternal thrombocytopenia

Introduction

Fetomaternal alloimmune thrombocytopenia is the platelet homologue of haemolytic disease of the newborn and, although relatively rare, it is the most common cause of severe perinatal thrombocytopenia. However, unlike haemolytic disease of the newborn, severe alloimmune thrombocytopenia occurs in the first pregnancy in 40–50% of cases and can cause significant morbidity and even mortality in the antenatal or postnatal period.

Discussion

This article reports the first case of fetomaternal thrombocytopenia as a result of the rare anti-human platelet antigen (HPA)-1b antibody, which was successfully treated antenatally. Fetomaternal thrombocytopenia occurs following maternal sensitization to paternal antigens (HPA) which are present on fetal platelets and is the most common cause of severe in-utero and neonatal thrombocytopaenia, especially in the first 72 hours following delivery (Roberts and Murray, 2003; Ghevaert et al, 2007).

The commonest causal antigen is HPA-1a (78% of cases), followed by HPA-5b (10%) and anti-HPA-15b (4%) (Spencer and Burrows, 2001; Ghevaert et al, 2007). Other rare antigens are HPA-3a, HPA-9 and HPA-1b (Winters et al, 1998; Morris et al, 2002).

There are 11 case studies in the literature reporting fetomaternal thrombocytopenia as a result of anti-HPA-1b antibodies (Kuijpers et al, 1994; Winters et al, 1998; Spencer and Burrows, 2001; Morris et al, 2002; Ghevaert et al 2007). Disease severity can vary from mild to severe. In at least three case studies the neonate had intracranial haemorrhage (Kuijpers et al, 1994). In all cases of fetomaternal thrombocytopenia the single most important risk factor appears to be a previously intracranial haemorrhage-affected sibling, with a recurrence rate of fetomaternal thrombocytopenia of up to 90% (Roberts and Murray, 2003). Hence, this patient was advised that her second pregnancy was high risk.

Table 1 shows the results of the laboratory investigations that confirmed the clinical diagnosis of fetomaternal thrombocytopenia. Genotype analysis showed that the mother and father had different HPA-1 genotypes. The baby had inherited his father's HPA-1 genotype (HPA 1a1b), and was therefore incompatible with the mother. The presence of maternal antibodies against HPA-1b was confirmed by the modified direct monoclonal antibody-specific immobilization of platelet antigens (MAIPA) assay, and was also demonstrated by cross-matching the paternal platelets against the maternal serum, which was positive for the anti-glycoprotein IIb/IIIa glycoprotein complex (which includes the HPA-1 antigen).

In all previous cases, fetomaternal thrombocytopenia caused by anti-HPA-1b

Table 1. Laboratory tests that confirmed fetomaternal alloimmune thrombocytopenia

Detection of maternal antibodies	Modified direct monoclonal antibody-specific immobilization of platelet antigens: positive immunoglobulin G to glycoprotein (GP) IIb/IIIa, but not to GPIb/IX, GPIa/IIa, or HLA class
Genotype identification	Maternal platelet genotype: human platelet antigen 1a1a, 2a2a, 3a3b, 5a5a
	Paternal platelet genotype: human platelet antigen 1a1b, 2a2a, 3a3b, 5a5a
	Baby's platelet genotype: human platelet antigen 1a1b, 2a2a, 3a3b, 5a5a
Detection of maternal–paternal serum incompatibility	Positive for anti-GPIIb/IIIa

Case Report

A 34-year old Caucasian woman (gravida 2, para 1) with a history of fetomaternal alloimmune thrombocytopenia presented for antenatal care in her second pregnancy at 12 weeks' gestation. Her first baby was severely affected by fetomaternal alloimmune thrombocytopenia (platelet count $< 3x10^9$/litre) and presented with neonatal purpura and fits caused by intracranial haemorrhage. Fetomaternal platelet incompatibility and presence of maternal anti-HPA-1b antibodies was demonstrated (*Table 1*) and the baby treated successfully, with platelet transfusions (HPA-1 negative).

During her second pregnancy, the mother's booking platelet count was 250 x 10^9/litre. Fetal platelet typing via amniocentesis at 16 weeks showed fetal platelet genotype HPA 1a1b. The modified direct monoclonal antibody-specific immobilization of platelet antigens (MAIPA) test showed that the mother was still positive for anti-HPA-1b antibodies (*Table 1*), indicating a high risk of fetomaternal alloimmune thrombocytopenia in this pregnancy. Starting at 16 weeks, she received weekly intravenous immunoglobulin 1 g/kg. The anomaly scan at 20 weeks was unremarkable. Further monitoring included weekly cranial scans to detect intracranial haemorrhage, and monthly growth scans. These were all normal. The mother declined fetal blood sampling to assess the fetal platelet count. Steroids were given at 33 weeks and baby delivered by planned caesarean section at 34 weeks. The boy weighed 2.75 kg and had no signs of bleeding. His platelet count was 100 x 10^9/litre and he has been well since.

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were treated postnatally with platelet transfusions and/or intravenous immunoglobulin. Therefore, recommendations regarding antenatal treatment are based on the treatment of anti-HPA-1a mediated fetomaternal thrombocytopenia.

In a randomized trial Berkowitz et al (2001) concluded that if the initial platelet count is less than 20 000/ml, or the previous child had a neonatal intracranial haemorrhage, the administration of intravenous immunoglobulin 1 g/kg/week plus prednisolone 1 mg/kg/day between 20 and 28 weeks gives statistically significant better results than intravenous immunoglobulin therapy alone. However, fetal blood sampling can result in fetal death in 1–1.3% of cases, while in-utero platelet transfusion has a morbidity of 5.5% and mortality of 1.3% (Berkowitz et al, 2006; Ghevaert et al, 2007).

The mother declined fetal blood sampling because of the associated risks and opted for intravenous immunoglobulin therapy alone. She was keen to avoid repeated steroid doses as prednisolone can also have maternal side effects, e.g. fluid retention, mood changes, weight gain and headaches, which may be enhanced when the therapies are combined (Berkowitz et al, 2006). Both parents felt postnatal treatment would be an option if antenatal treatment failed.

Conclusions

The case discussed here is the first prenatal identification and successful treatment of HPA-1b antibody-mediated fetomaternal thrombocytopenia. The authors therefore conclude that anti-HPA-1b antibody-mediated fetomaternal thrombocytopenia is amenable to prenatal intravenous immunoglobulin therapy alone. **BJHM**

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