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Fetal and neonatal alloimmune thrombocytopenia in siblings

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Fetal and neonatal alloimmune thrombocytopenia (FNAIT) is a rare condition, with a prevalence of 1 in 1,000–1,500 pregnancies [1, 2]. It is caused by IgG antibodies against fetal human platelet alloantigens (HPA). In Caucasian populations, the most commonly detected antibody is anti-HPA-1a, responsible for c.80–90% of cases [3, 4].

Maternal anti-HPA antibodies passing through the placenta destroy fetal platelets (PLT), which can result in severe bleeding complications such as intracranial hemorrhages (ICH) [5]. Indubitably, the clinical presentation of FNAIT depends on the level of platelets. In most cases, the symptoms are mild — possibly asymptomatic — consisting usually of petechiae, ecchymoses or bruises notice in the first hours of life [2]. Clinicians considering a differential diagnosis of neonates with thrombocytopenia should bear in mind FNAIT as a possible cause of symptoms. This can occur in the early stages of a first pregnancy, and subsequent fetuses of the same parents can be affected as well. Here, we present the cases of siblings diagnosed with FNAIT, who were born two years apart. The first, male, neonate was born on time at 40 weeks' gestation by cesarean section due to no progress in labor, in a good condition, given 10 points on the Apgar scale, and weighing 3,180 g. There were no complications during the pregnancy. At the first examination, widespread petechiae and bruises on the whole body were detected. Twice repeated laboratory test results showed severe thrombocytopenia: PLT 14,000/μL and 10,000/μL. Head ultrasound did not show any abnormalities, and no other bleeding complication of a low amount of platelets was discovered. PLT were transfused with good effect, and from day six of life, when the level of platelets decreased again, intravenous immunoglobulins (IVIg) (Privigen®) were administered. Infections were ruled out. The amount of PLT increased over the following days (Table I), reaching 285,000/μL at discharge. No specific cause of thrombocytopenia was established, but the parents were advised to seek a hematological consultation.

During her second pregnancy, the mother visited the Hematology Clinic for Pregnant Women in Warsaw, Poland. HPA types were analyzed. An allele-specific polymerase chain reaction (PCR) was performed to determine the genotype of platelet antigens. She carried HPA-1b, -2a, -3a, -4a, -5a, -6a, -9a, and -15a, and the child's father carried HPA-1a, -2a, -2b, -3a, -4a, -5a, -6a, -9a, and -15b. 100% incompatibility in the antigens HPA-1a and HPA-15b were detected between the parents, and 50% incompatibility in the antigen HPA-2b.

In the mother's blood sample, anti-HPA-1a antiplatelet antibodies (titer 1:64 with activity 23.17 IU/mL) targeting the platelet glycoprotein (GP) IIb/IIIa were found.

The second sibling — a girl — was born prematurely at 36 weeks' gestation, by cesarean section to avoid labor injuries, when regular contractions of the uterus had appeared. Birth weight was 2,570 g. During the pregnancy, from week 20 onwards the mother was given prophylactically intravenous immunoglobulins weekly and regular fetal ultrasounds were performed to monitor for complications, e.g. ICH. The girl soon after birth was assessed as 7 points on the Apgar scale and needed ventilation support with Neopuff during the first three minutes of life. Her state gradually improved during an observation in the Neonatology Intensive Care Unit. On physical examination, numerous bruises were detected. The laboratory results showed severe thrombocytopenia: 12,000/μL. Therapy with IVIg (Pentaglobin®) was started instantly, and platelet concentrate was ordered. Due to premature labor and a lack of

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Table I. Children's platelets count results and their treatments

Day of life	First child's platelets count results [/μL] and treatment		Second child's platelets count results [/μL] and treatment	
1	14,000 10,000	Platelet transfusion	12,000 110,000 79,000	Platelet transfusion and administration of IVIg
2	43,000 50,000	–	132,000	Administration of IVIg
3	52,000	–	122,000	Administration of IVIg
4	–	–	82,000	–
5	–	–	142,000	–
6	29,000 31,000	Administration of IVIg	–	–
7	58,000	Administration of IVIg	82,000	–
8	90,000	Administration of IVIg	247,000	–
9	124,000	Administration of IVIg	246,000	–
12	285,000	–	–	–

IVIg – intravenous immunoglobulins

individually attuned preparation, a universal platelet concentrate was transfused. After a few hours, platelets collected from the mother were also administered. The immunoglobulins were given again twice over the next two days. There was no bleeding to the brain and abdomen detected by a control ultrasound. The level of thrombocytes stabilized over subsequent days of hospitalization. When the child was discharged from the Neonatology Department, in good condition after nine days, the amount of platelets was 246,000/μL (Table I).

At present, no standard screening for FNAIT is recommended. Nevertheless, experts have suggested that such population screening would reduce morbidity and mortality associated with this condition [3, 5, 6]. The early identification of pregnancies at risk is essential in preventing major bleeding in fetuses and babies. When FNAIT is suspected, thorough diagnostic tests should be performed to enable proper fetal management [6]. Antenatal treatment of FNAIT requires the administration of intravenous immunoglobulins to mothers and regular control ultrasounds of fetuses [2, 7]. An elective near term cesarean section is the preferred mode of delivery in order to minimize the risk of bleeding complications [2, 4]. Also, postnatally in children diagnosed with FNAIT, platelets are being transfused when severe thrombocytopenia is discovered in laboratory results, and IVIg are given as well [1, 3, 7].

Authors' contributions

AWA, ABG prepared manuscript, with contributions from ISK, AZS.

Conflict of interest

The authors declare no conflict of interest.

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Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; EU Directive 2010/63/EU for animal experiments and uniform requirements for manuscripts submitted to biomedical journals.

References

1. Stam W, Wachholz GE, de Pereda JM, et al. Fetal and neonatal alloimmune thrombocytopenia: current pathophysiological insights and perspectives for future diagnostics and treatment. Blood Rev. 2023; 59: 101038, doi: 10.1016/j.blre.2022.101038, indexed in Pubmed: 36581513.
2. de Vos TW, Winkelhorst D, de Haas M, et al. Epidemiology and management of fetal and neonatal alloimmune thrombocytopenia. Transfus Apher Sci. 2020; 59(1): 102704, doi: 10.1016/j.transci.2019.102704, indexed in Pubmed: 31974030.
3. Salomon O, Rosenberg N. Predicting risk severity and response of fetal neonatal alloimmune thrombocytopenia. Br J Haematol. 2013; 162(3): 304–312, doi: 10.1111/bjh.12372, indexed in Pubmed: 23672281.
4. Tiller H, Husebekk A, Ahlen MT, et al. Current perspectives on fetal and neonatal alloimmune thrombocytopenia - increasing clinical concerns and new treatment opportunities. Int J Womens Health. 2017; 9: 223–234, doi: 10.2147/IJWH.S90753, indexed in Pubmed: 28458583.
5. Winkelhorst D, Kamphuis MM, Steggerda SJ, et al. Perinatal outcome and long-term neurodevelopment after intracranial haemorrhage due to fetal and neonatal alloimmune thrombocytopenia. Fetal Diagn Ther. 2019; 45(3): 184–191, doi: 10.1159/000488280, indexed in Pubmed: 29730660.
6. Lieberman L, Greinacher A, Murphy MF, et al. International Collaboration for Transfusion Medicine Guidelines (ICTMG). Fetal and neonatal alloimmune thrombocytopenia: recommendations for evidence-based practice, an international approach. Br J Haematol. 2019; 185(3): 549–562, doi: 10.1111/bjh.15813, indexed in Pubmed: 30828796.
7. Winkelhorst D, Murphy MF, Greinacher A, et al. Antenatal management in fetal and neonatal alloimmune thrombocytopenia: a systematic review. Blood. 2017; 129(11): 1538–1547, doi: 10.1182/blood-2016-10-739656, indexed in Pubmed: 28130210.