Letter to the editor

*Old tools revisited give hope - new treatment option for families with a history of severe FNAIT complications*

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Fetal and neonatal alloimmune thrombocytopenia (FNAIT) is defined as fetal and neonatal thrombocytopenia caused by maternal alloantibodies directed against fetal platelets due to incompatibility between fetal and maternal platelet antigens (HPAs). The majority of FNAIT cases are caused by anti-HPA-1a antibodies(1). FNAIT is the most common cause of intracranial hemorrhage (ICH) in otherwise healthy term newborns, affecting 1:12,500 – 1:25,000. The clinical outcome of FNAIT-related ICH is typically poor, and the risk of recurrence in subsequent pregnancies is high(2;3). FNAIT is also associated with increased risk of miscarriage, low birth weight, and stillbirth(1;4).

Children with FNAIT are typically diagnosed unexpectedly and shortly after delivery. Current treatment protocols vary between countries, but most western countries offer antenatal IVIg given as weekly doses from 2nd trimester until delivery in pregnancies where the risk of FNAIT is known. **IVIg treatment is considered effective when the neonatal platelet count in a subsequent pregnancy is increased compared with the previous FNAIT pregnancy.** However, the natural course of FNAIT in several subsequent pregnancies was recently reported for the first time, questioning the effect of antenatal IVIG treatment on neonatal platelet counts(5). The effect of IVIg in preventing severe FNAIT regarding neonatal platelet count is therefore debatable, but it is generally agreed that IVIg reduces the risk of ICH recurrence from 70-80% risk without treatment to about 10% with IVIg(3).

A Norwegian woman born 1979 had a child affected by severe FNAIT after her first pregnancy in 2002. At that time, she participated in a large Norwegian screening study(1) and was therefore identified already in the 1st trimester to have the rarer platelet antigen type HPA-1bb. She developed high levels of anti-HPA-1a antibodies targeting the fetus’ platelets at 24 weeks of pregnancy. The newborn had platelet count below $5 \times 10^9$/L and widespread skin bleedings at birth, and was transfused with compatible platelets shortly after delivery by cesarean section. She has since repeatedly tried to conceive with her HPA-1 discordant husband, but miscarried five pregnancies during the 1st trimester. We found a solution for this couple, which we believe could be a treatment option for other families in similar situation.

**After obtaining approval by the Norwegian Directorate of Health**, we genotyped 50 open-identity sperm donors and identified a donor with the compatible platelet antigen HPA-1bb.
Our patient conceived after in vitro fertilization using sperm from the selected donor. She had an uneventful singleton pregnancy despite high and stable maternal serum levels of anti-HPA-1a antibodies. No maternal anti-HLA class 1 antibodies were detected. A healthy newborn with normal platelet count (300 × 10⁹/L) was delivered by elective cesarean section at 38 weeks of pregnancy. The patient described has given written approval of the content.

We acknowledge the potential ethical challenges and concerns that this management option for FNAIT raise. It is important to consider if a woman has other alloantibody specificities in addition to anti-HPA-1a before undergoing this treatment, for example anti-HLA class 1 antibodies. Nonetheless, we consider use of HPA-1-matched donor sperm as a safe and possible treatment for the minority of HPA-1bb women with history of recurrent devastating FNAIT-related complications, including ICH. The alternative choice for these couples would often be to refrain from further pregnancies.

Conflict of Interest

B.S. has financial relationship with Prophylix Pharma AS, a company working to develop a prophylaxis for FNAIT

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Reference List


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