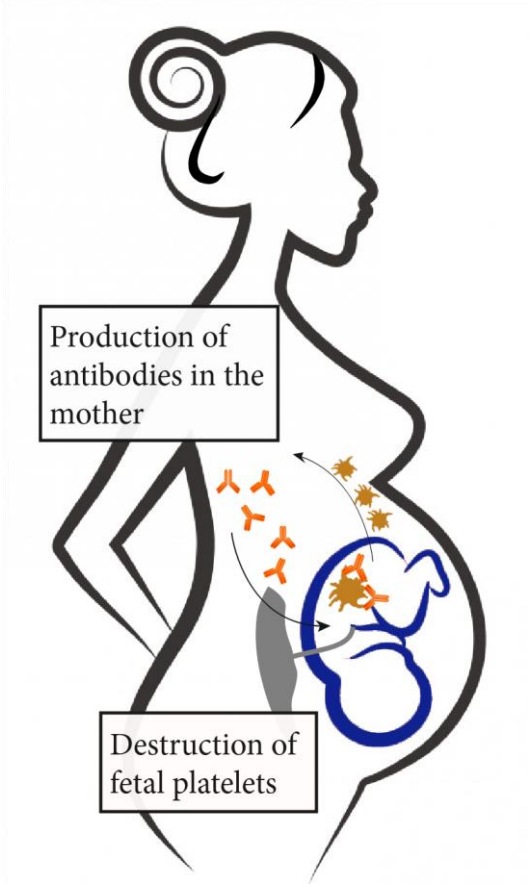
Fetal/neonatal alloimmune thrombocytopenia (FNAIT)

Introduction

Fetal/neonatal alloimmune thrombocytopenia (FNAIT) is a rare disorder that affects platelets in fetus and newborn. Platelets are small blood cells that help to form blood clots, and lack of platelets increases the baby's risk of bleeding. FNAIT occurs in approximately 1/1000 pregnancies.

All platelets express surface proteins important for their function. These can differ slightly between individuals and these differences make up what are referred to as human platelet antigens (HPAs). There are many types of HPAs, and the expression of these determine your platelet type. Children inherit their platelet type from both parents.



During all pregnancies, a small amount of fetal blood, including platelets, enter the mother's circulation, usually without any ill effects.

In FNAIT, however, fetal antigens inherited from the father trigger the mother's immune system to produce antibodies against fetal platelets. These antibodies cross the placenta into the fetal circulation and bind the baby's platelets. Fetal platelets coated with maternal antibodies are eliminated, and the baby may develop thrombocytopenia (low platelet count) with increased risk of bleeding. Intracranial hemorrhage is a dreaded, but rare, complication.

The antibodies described above are called HPA antibodies. About 2% of the population have the uncommon platelet type (HPA1bb), and may produce anti-HPA-1a antibodies, which is the most common HPA antibody in Whites. Among HPA-1bb pregnant women, approximately 10% develop anti-HPA-1a antibodies, and about 1% deliver babies with thrombocytopenia.
Likewise, there are other platelet antibodies that also can cause FNAIT, and although not frequently found, they are tested for as in the routine laboratory work up.

Laboratory investigation of FNAIT is performed at the Norwegian National Unit for Platelet Immunology (NNUPI) at the University Hospital of North Norway.

Evaluation

FNAIT is a rare disease, and currently there are no established screening programs to identify pregnancies at risk. Thus, FNAIT is often diagnosed after delivery.

Doctors may suspect FNAIT if the newborn displays:

• Skin patches/ rash caused by bleeding (petechiae or ecchymosis)
• Other bleeding
• Thrombocytopenia (lack of platelets) in laboratory workup An FNAIT diagnosis can only be confirmed after analysis of blood samples from the mother and her newborn, and preferably also the father. The investigation includes determination of platelet types and identification of platelet the antibodies.

Risk of FNAIT is identified if the pregnant woman:

- Previously has given birth to a child with FNAIT
- Is aware that she has an uncommon platelettype HPA-1bb (e.g. registrated as blood donor or has a close relative who has given birth to a child with FNAIT).

- Pregnant women at risk of delivering a child with FNAIT are monitored regularly during pregnancy according to the Norwegian FNAIT management program.[1,2] Blood samples from the mother are analyzed for platelet antibodies (HPA antibodies) in pregnancy weeks 20-23 and 34, as well as 6 weeks after delivery. If HPA antibodies are found, the levels are monitored more often, and the mother is offered a clinical examination including evaluation with fetal ultrasound by an obstetrician.

Treatment

The platelet number in the baby often correlates with the amount of maternal antibodies. If the antibody level is equal or above 3 IU/mL the pregnant women is offered caesarean section 1-2 weeks before term. For pregnant women with low levels of anti-HPA-1a, there is generally no indication for caesarian section. If the pregnant woman previously has given birth to a child with FNAIT and intracranial hemorrhage, she is offered treatment with weekly high-dose intravenous immunoglobulins from pregnancy week 20.

After delivery, the baby's platelet count is measured. When the platelet count is low or the baby has signs of bleeding, the baby usually receives platelet transfusion, preferably with HPA-compatible platelets. The transfused platelets help normalizing the baby's platelet count and prevent bleeding complications. Also, when the platelet count is low, the doctors perform an ultrasound evaluation of the baby´s brain to look for bleeding. In some cases, the baby is also treated with immunoglobulins. It is safe to breastfeed the baby.

Follow-up

Children born with FNAIT without serious bleeding complications recover completely, and normally do not require further follow-up after leaving the hospital. After delivery the maternal antibodies are rapidly cleared from the baby's blood and the platelet count usually normalizes within a week. In case of

complications such as intracranial hemorrhage, the baby will receive appropriate treatment and follow-up by pediatricians.

All women with the rare blood type HPA-1bb are recommended to take a blood test 6 weeks after delivery, to evaluate antibody status. These HPA-1a-immunized women are followed according to the Norwegian FNAIT management program[1, 2] in subsequent pregnancies. The platelet antibodies are also of importance if these women should require a blood transfusion in the future. Ideally, women with platelet antibodies should receive blood from donors with the same platelet type. However, in case of emergency and if such blood products are not available, it is considered safe to transfuse blood from an unmatched donor. Women with platelet antibodies are not accepted as blood donors.

For more information, please contact the Norwegian National Unit for Platelet Immunology (NNUPI)

www.unn.no/nnupi

Phone: +47 776 28086 E-mail: blodplatelab@unn.no

References:

1. Tiller H, Ahlen MT, Akkök CA, Husebekk A. Fetal and neonatal alloimmune thrombocytopenia – the Norwegian management model, Transfus Apher Sci (2020) DOI: 10.1016/j.transci.2019.102711
2. Tiller et al. Alloimmunisering mot trombocytt-antigener (inkl FNAIT). Veileder i fødselshjelp (2020). ePub. ISBN 978-82- 692382-0-4. (In Norwegian)