Platelet Antigen Genotyping Panel

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Human platelet antigen (HPA) genotyping is used for fetal or neonatal testing following detection of unexplained intracranial hemorrhage (ICH) or thrombocytopenia, which raises suspicion for neonatal alloimmune thrombocytopenia (NAIT; also referred to as perinatal alloimmune thrombocytopenia [PAT]).

Maternal and paternal testing is performed when the fetus or neonate is suspected to have NAIT. Women who have had a previously affected pregnancy, have a history of posttransfusion purpura, or have a sister with a previously affected pregnancy are candidates for this testing.

Featured ARUP Testing

Platelet Antigen Genotyping Panel 3000193

Method: Polymerase Chain Reaction (PCR)/Fluorescence Monitoring

- Use in risk assessment for NAIT
- May be ordered for parental or neonatal genotyping
- For fetal testing, order Platelet Antigen Genotyping Panel, Fetal (3016673) using a fetal specimen.

Disease Overview

Incidence

NAIT is the most common cause of severe thrombocytopenia in healthy term neonates and occurs in 0.3-1/1000 births.[1]

- In White individuals, 80% of NAIT is caused by maternal antibodies directed against HPA-1a and approximately 20% is caused by antibodies directed against HPA-5b[2]
- Posttransfusion purpura is estimated to occur in 1/50,000-100,000 transfusions.[3]

Symptoms

Symptoms of NAIT can include[4]:

- Severe thrombocytopenia in an otherwise healthy newborn
- ICH in utero, at birth, or postnatally
  - Estimated to affect 7–26% of neonates with NAIT
  - ICH is fatal in 1–10% of affected neonates
  - 14–26% of ICH survivors have neurologic sequelae (eg, intellectual disability, seizures, cerebral palsy, or cortical blindness)
- Widespread petechiae or ecchymoses
- Hematoma development at injection sites
- Bleeding after circumcision

Diagnostic Issues

- NAIT results from maternal alloimmunization to paternally inherited fetal platelet antigen; maternal alloantibodies cross the placenta and cause fetal platelet destruction and thus, fetal thrombocytopenia[5]
- Because prenatal platelet typing is not routinely performed, at-risk women are typically identified only after an affected pregnancy, although some may be identified through screening because of a sister with an affected pregnancy[6]
- Recurrence risk is approximately 85%[7] and severity may increase in subsequent pregnancies[8]
- Posttransfusion purpura is typically caused by HPA-1a antibodies in a previously sensitized HPA-1a-negative patient who is reexposed to the alloantigen as a result of transfusion[5]
- Clinical correlation between antibody titers and NAIT occurrence is not reliable[4]
- Specific paternal platelet antigens may not react with alloantibodies; genotyping allows for more accurate risk assessment and better pregnancy management
- Testing may be helpful to
  - Screen for neonatal immunization during pregnancy when parents had a previously affected pregnancy or when unexplained ICH is detected
  - Assess risk of NAIT in future pregnancies
  - Assess risk of posttransfusion purpura and thrombocytopenia

Genetics

Genes

HPA genes (*ITGB3*, *GP1BA*, *ITGA2B*, *ITGA2*, and *CD109)*

Alleles

- Approximately 29 different types of platelet-specific alloantigens have been identified[9]
- The more common allele is designated as “a” and the less common allele is known as “b”[9]
  - 1.6% to 4.6% of the general population are homozygous for HPA-1b[4]
  - These women are at risk for alloimmunization during pregnancy if they have a reproductive partner who is homozygous for HPA-1a or heterozygous for HPA-1a/b and contributes the HPA-1a allele to the fetus

Test Description

Multiplex polymerase chain reaction (PCR) followed by fluorescence monitoring to detect HPA alleles:

Antigen	Gene and Glycoprotein	Allele
HPA-1	*ITGB3*, GPIIIa	c.176T>C, p.L59P
HPA-2	*GP1BA*, GPIba	c.482C>T, p.T161M
HPA-3	*ITGA2B,* GPIIb	c.2621T>G, p.I874S
HPA-4	*ITGB3,* GPIIIa	c.506G>A, p.R169Q
HPA-5	*ITGA2,* GPIa	c.1600G>A, p.E534K
HPA-6	*ITGB3,* GPIIIa	c.1544G>A, p.R515Q
HPA-15	*CD109,* CD109	c.2108C>A, p.S703Y

Test Interpretation

Sensitivity/Specificity

- Clinical sensitivity and specificity are variable; dependent on ethnicity
- Analytic sensitivity and specificity are 99%

Results

- HPA-a/a homozygous
  - Two copies of the common “a” allele
- HPA-a/b heterozygous
  - One copy of the common “a” allele and one copy of the less common “b” allele
- HPA-b/b homozygous
  - Two copies of the less common “b” allele

Limitations

- HPA genes and variants, other than those tested, will not be detected
- Bloody amniotic fluid specimens may give false-negative results due to maternal cell contamination
- Diagnostic errors can occur due to rare sequence variations

References

1. Lieberman L, Greinacher A, Murphy MF, et al. Fetal and neonatal alloimmune thrombocytopenia: recommendations for evidence-based practice, an international approach. *Br J Haematol*. 2019;185(3):549-562.

2. Regan F, Lees CC, Jones B, et al. Prenatal management of pregnancies at risk of fetal neonatal alloimmune thrombocytopenia (FNAIT): Scientific Impact Paper No. 61. *BJOG*. 2019;126(10):e173-e185.

3. Metcalfe P. Platelet antigens and antibody detection. *Vox Sang*. 2004;87 Suppl1:82-86.

4. Espinoza JP, Caradeux J, Norwitz ER, et al. Fetal and neonatal alloimmune thrombocytopenia. *Rev Obstet Gynecol*. 2013;6(1):e15-e21.

5. Heikal NM, Smock KJ. Laboratory testing for platelet antibodies. *Am J Hematol*. 2013;88(9):818-821.

6. Winkelhorst D, Oepkes D, Lopriore E. Fetal and neonatal alloimmune thrombocytopenia: evidence based antenatal and postnatal management strategies. *Expert Rev Hematol*. 2017;10(8):729-737.

7. Mella MT, Eddleman KA. Neonatal alloimmune thrombocytopenia. *Intern J Clin Trans Med*. 2015;3;29-40.

8. Bertrand G, Kaplan C. How do we treat fetal and neonatal alloimmune thrombocytopenia? *Transfusion*. 2014;54(7):1698-1703.

9. European Molecular Biology Laboratory-European Bioinformatics Institute (EMBL-EBI). Immuno Polymorphism Database. Accessed Apr 2020.

Related Information

Neonatal Alloimmune Thrombocytopenia - NAIT
Thrombocytopenic Disorders

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