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Congenital amegakaryocytic thrombocytopenia

What is congenital amegakaryocytic thrombocytopenia?

Congenital amegakaryocytic thrombocytopenia is an inherited disease characterized by bone marrow failure.[1,2] Individuals with congenital amegakaryocytic thrombocytopenia have reduced or nonfunctional thrombopoietin (TPO) receptor proteins.[2] The TPO receptor protein promotes the growth and division of megakaryocytes, which produce platelets, the cells involved in blood clotting.[2] The TPO receptor also helps maintain hematopoietic stem cells, which are cells that can potentially change into red blood cells, white blood cells, and platelets.[2] Signs and symptoms of congenital amegakaryocytic thrombocytopenia are due to abnormalities in the TPO receptor protein.[3]

What are the symptoms of congenital amegakaryocytic thrombocytopenia and what treatment is available?

Congenital amegakaryocytic thrombocytopenia is a disease with variable severity and age at onset. Symptoms typically begin in infancy[2, 3] and may include:[1, 2, 3]

- Megakaryocytopenia (low numbers of megakaryocytes, giant cells found in the bone marrow)
- Thrombocytopenia (low numbers of platelets)
- Pancytopenia (reduced numbers of red cells, white cells, and platelets)
- Bleeding, including cutaneous, gastrointestinal, pulmonary, and intracranial hemorrhage

The more severe form of congenital amegakaryocytic thrombocytopenia is known as Type I; individuals with Type 1 have no TPO receptor protein function and have continuously low platelet counts with early onset of pancytopenia.[1] Individuals with Type II congenital amegakaryocytic thrombocytopenia have some functional TPO receptor protein, have a brief increase in platelet counts during the first year of life, and may have later onset of bone marrow failure.[1, 2]

Primary treatments are bone marrow transplantation[3] or hematopoietic stem cell transplantation.[3]

How is congenital amegakaryocytic thrombocytopenia inherited?

Congenital amegakaryocytic thrombocytopenia is an autosomal recessive disease caused by mutations in the *MPL* gene.[2] An individual who inherits one copy of an *MPL* gene mutation is a carrier and is not expected to have related health problems. An individual who inherits two *MPL* mutations, one from each parent, is expected to be affected with congenital amegakaryocytic thrombocytopenia.

If both members of a couple are carriers of mutations in the same gene, the risk for an affected child is 25% in each pregnancy; therefore, it is especially important that the reproductive partner of a carrier be offered testing.

Who is at risk for congenital amegakaryocytic thrombocytopenia?

Congenital amegakaryocytic thrombocytopenia is a rare condition with an unknown worldwide prevalence. It may be seen more commonly among the Ashkenazi Jewish population with a 1 in 75 carrier frequency.[4]

Having a relative who is a carrier or who is affected can increase an individual's risk to be a carrier. Consultation with a genetics health professional may be helpful in determining carrier risk and appropriate testing.

What does a positive test result mean?

If a gene mutation is identified, an individual should speak to a physician or genetics health professional about the implications of the result and appropriate testing for the reproductive partner and at-risk family members.

What does a negative test result mean?

A negative result reduces, but does not eliminate, the possibility that an individual carries a gene mutation. The likelihood of being a carrier is also influenced by family history, medical symptoms, and other relevant test results.

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Where can I get more information?

Platelet Disorder Support Association: http://www.pdsa.org/

Jewish Genetic Diseases: http://www.mazornet.com/genetics/camt.htm

References

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3. Al-Qahtani, F.S. Congenital Amegakaryocytic Thrombocytopenia: A Brief Review of the Literature. Clin Med InSights Pathol. 2010; 3:25-30.
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