What is congenital amegakaryocytic thrombocytopenia?

Congenital amegakaryocytic thrombocytopenia is an inherited disease characterized by bone marrow failure.⁵ Individuals with congenital amegakaryocytic thrombocytopenia have reduced or nonfunctional thrombopoietin (TPO) receptor proteins.³ The TPO receptor protein promotes the growth and division of megakaryocytes, which produce platelets, the cells involved in blood clotting.³ 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.³ Signs and symptoms of congenital amegakaryocytic thrombocytopenia are due to abnormalities in the TPO receptor protein.⁵

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 infancy²,³ 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 I 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 transplantation³ 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.
Where can I get more information?


Jewish Genetic Diseases:  [http://www.mazornet.com/genetics/camt.htm](http://www.mazornet.com/genetics/camt.htm)

References