Ataxia-pancytopenia syndrome

Description

Ataxia-pancytopenia syndrome is a rare condition that affects the part of the brain that coordinates movement (the cerebellum) and blood-forming cells in the bone marrow. The age when signs and symptoms begin, the severity of the condition, and the rate at which it worsens all vary among affected individuals.

People with ataxia-pancytopenia syndrome have neurological problems associated with a loss of tissue (atrophy) and other changes in the cerebellum. These problems include poor coordination and balance (ataxia), difficulty with movements that involve judging distance or scale (dysmetria), uncontrollable muscle contractions (clonus), and involuntary back-and-forth eye movements (nystagmus). These neurological issues worsen over time, making walking and other movements challenging. Some affected individuals eventually require wheelchair assistance.

Ataxia-pancytopenia syndrome also causes a shortage of one or more types of normal blood cells: red blood cells, white blood cells, and platelets. A shortage of all three of these cell types is known as pancytopenia. Pancytopenia can result in extreme tiredness (fatigue) due to low numbers of red blood cells (anemia), frequent infections due to low numbers of white blood cells (neutropenia), and abnormal bleeding due to low numbers of platelets (thrombocytopenia). Ataxia-pancytopenia syndrome is also associated with an increased risk of certain cancerous conditions of the blood, particularly myelodysplastic syndrome and acute myeloid leukemia.

Frequency

Ataxia-pancytopenia syndrome appears to be very rare. At least 25 affected individuals from four families have been described in the medical literature.

Causes

Ataxia-pancytopenia syndrome is caused by inherited mutations in the *SAMD9L* gene. The protein produced from this gene is involved in regulating the growth and division (proliferation) and maturation (differentiation) of cells, particularly cells in the bone marrow that give rise to blood cells. Studies suggest that the SAMD9L protein acts as a tumor suppressor, keeping cells from growing and dividing too rapidly or in an uncontrolled way. The SAMD9L protein also appears to play an important role in the

brain, particularly the cerebellum, although less is known about the protein's function there.

The mutations that cause ataxia-pancytopenia syndrome are described as "gain-of-function." They increase the SAMD9L protein's ability to block cell growth and division. In the bone marrow, the resulting reduction in cell proliferation leads to a shortage of red blood cells, white blood cells, and platelets. It is unclear how the effects of these mutations are related to ataxia and the other neurological problems associated with ataxia-pancytopenia syndrome.

It seems paradoxical that gain-of-function mutations in the *SAMD9L* gene, which enhance the protein's tumor suppressor function, could increase the risk of developing cancerous conditions such as myelodysplastic syndrome and acute myeloid leukemia. It appears that certain cells in the bone marrow with an inherited gain-of-function *SAMD9L* gene mutation can develop additional genetic changes that are associated with milder pancytopenia but an increased cancer risk. These changes include mutations that disable the *SAMD9L* gene ("loss-of-function" mutations) or a deletion of part of the long (q) arm of chromosome 7 that contains the *SAMD9L* gene. These additional changes compensate for the effects of the gain-of-function mutation in bone marrow cells. They prevent an overactive SAMD9L protein from excessively restricting cell proliferation, which reduces the severity of pancytopenia in affected individuals. However, a loss of the *SAMD9L* gene and other genes on the long arm of chromosome 7 may allow cells to grow and divide uncontrollably, leading to cancer. A deletion of the long arm of chromosome 7 is a well-known risk factor for myelodysplastic syndrome and leukemia.

Learn more about the gene associated with Ataxia-pancytopenia syndrome

- SAMD9L

Inheritance

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. In all reported cases, an affected person has had one parent with the condition.

Other Names for This Condition

- ATXPC
- Myelocerebellar disorder

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Ataxia-pancytopenia syndrome (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1327919/)

Genetic and Rare Diseases Information Center

- Ataxia-pancytopenia syndrome (https://rarediseases.info.nih.gov/diseases/3865/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Catalog of Genes and Diseases from OMIM

- ATAXIA-PANCYTOPENIA SYNDROME; ATXPC (https://omim.org/entry/159550)
- MONOSOMY 7 MYELODYSPLASIA AND LEUKEMIA SYNDROME 1; M7MLS1 (https://omim.org/entry/252270)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28ataxia-pancytopenia%5BTIAB%5D%29+OR+%28%28ataxia%5BTIAB%5D%29+AND+%28pancytopenia%5BTIAB%5D%29+AND+%28monosomy+7%5BTIAB%5D%29%29+OR+%28myelocerebellar+disorder%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D)

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