X-linked thrombocytopenia

X-linked thrombocytopenia is a bleeding disorder that primarily affects males. This condition is characterized by a blood cell abnormality called thrombocytopenia, which is a shortage in the number of blood cell fragments involved in clotting (platelets). Affected individuals often have abnormally small platelets as well, a condition called microthrombocytopenia. X-linked thrombocytopenia can cause individuals to bruise easily or have episodes of prolonged bleeding following minor trauma or even in the absence of injury (spontaneous bleeding). Some people with this condition experience spontaneous bleeding in the brain (cerebral hemorrhage), which can cause brain damage that can be life-threatening.

Some people with X-linked thrombocytopenia also have patches of red, irritated skin (eczema) or an increased susceptibility to infections. In severe cases, additional features can develop, such as cancer or autoimmune disorders, which occur when the immune system malfunctions and attacks the body’s own tissues and organs. It is unclear, however, if people with these features have X-linked thrombocytopenia or a more severe disorder with similar signs and symptoms called Wiskott-Aldrich syndrome.

Some people have a mild form of the disorder called intermittent thrombocytopenia. These individuals have normal platelet production at times with episodes of thrombocytopenia.

Frequency

The estimated incidence of X-linked thrombocytopenia is between 1 and 10 per million males worldwide; this condition is rarer among females.

Causes

Mutations in the WAS gene cause X-linked thrombocytopenia. The WAS gene provides instructions for making a protein called WASP. This protein is found in all blood cells. WASP is involved in relaying signals from the surface of blood cells to the actin cytoskeleton, which is a network of fibers that make up the cell's structural framework. WASP signaling activates the cell when it is needed and triggers its movement and attachment to other cells and tissues (adhesion). In white blood cells, which protect the body from infection, this signaling allows the actin cytoskeleton to establish the interaction between cells and the foreign invaders that they target (immune synapse).

WAS gene mutations that cause X-linked thrombocytopenia typically lead to the production of an altered protein. The altered WASP has reduced function and cannot efficiently relay signals from the cell membrane to the actin cytoskeleton. In people with X-linked thrombocytopenia, these signaling problems primarily affect platelets, impairing their development. In some cases, white blood cells are affected. When WASP function
is impaired in white blood cells, they are less able to respond to foreign invaders and immune problems such as infections, eczema, and autoimmune disorders can occur.

Inheritance Pattern

This condition is inherited in an X-linked pattern. The gene associated with this condition is located on the X chromosome, which is one of the two sex chromosomes. In females (who have two X chromosomes), a mutation in one of the two copies of the gene in each cell may or may not cause the disorder. In males (who have only one X chromosome), a mutation in the only copy of the gene in each cell causes the disorder. In most cases of X-linked inheritance, males experience more severe symptoms of the disorder than females. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

Other Names for This Condition

• thrombocytopenia 1
• XLT

Diagnosis & Management

Genetic Testing Information

• What is genetic testing? /primer/testing/genetictesting

Research Studies from ClinicalTrials.gov

• ClinicalTrials.gov https://clinicaltrials.gov/ct2/results?cond=%22X-linked+thrombocytopenia%22

Other Diagnosis and Management Resources


Additional Information & Resources

Health Information from MedlinePlus

• Encyclopedia: Thrombocytopenia https://medlineplus.gov/ency/article/000586.htm
• Health Topic: Platelet Disorders https://medlineplus.gov/plateletdisorders.html
Genetic and Rare Diseases Information Center

- X-linked thrombocytopenia
  https://rarediseases.info.nih.gov/diseases/5176/x-linked-thrombocytopenia

Additional NIH Resources

- National Heart Lung and Blood Institute: Thrombocytopenia
  https://www.nhlbi.nih.gov/health-topics/thrombocytopenia

Educational Resources

- Johns Hopkins Medicine: What are Platelets and Why are They Important?
  https://www.hopkinsmedicine.org/heart_vascular_institute/clinical_services/
  centers_excellence/womens_cardiovascular_health_center/patient_information/
  health_topics/platelets.html
- Merck Manual Consumer Version: Thrombocytopenia
  https://www.merckmanuals.com/home/blood-disorders/platelet-disorders/overview-
  of-thrombocytopenia
- Orphanet: X-linked thrombocytopenia with normal platelets
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=852

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD): WAS Related Disorders
  https://rarediseases.org/rare-diseases/was-related-disorders/
- Platelet Disorder Support Association: Platelet Details
  https://www.pdsa.org/about-itp/platelet-details.html
- The Wiskott-Aldrich Foundation
  http://www.wiskott.org/

Clinical Information from GeneReviews

- WAS-Related Disorders
  https://www.ncbi.nlm.nih.gov/books/NBK1178

Scientific Articles on PubMed

- PubMed
  %5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+
  %22last+3600+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- THROMBOCYTOPENIA 1
  http://omim.org/entry/313900
Sources for This Summary


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Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services