Weill-Marchesani syndrome

Weill-Marchesani syndrome is a disorder of connective tissue. Connective tissue forms the body's supportive framework, providing structure and strength to the muscles, joints, organs, and skin.

The major signs and symptoms of Weill-Marchesani syndrome include short stature, eye abnormalities, unusually short fingers and toes (brachydactyly), and joint stiffness. Adult height for men with Weill-Marchesani syndrome ranges from 4 feet, 8 inches to 5 feet, 6 inches. Adult height for women with this condition ranges from 4 feet, 3 inches to 5 feet, 2 inches.

An eye abnormality called microspherophakia is characteristic of Weill-Marchesani syndrome. This term refers to a small, sphere-shaped lens, which is associated with nearsightedness (myopia) that worsens over time. The lens also may be positioned abnormally within the eye (ectopia lentis). Many people with Weill-Marchesani syndrome develop glaucoma, an eye disease that increases the pressure in the eye and can lead to blindness.

Occasionally, heart defects or an abnormal heart rhythm can occur in people with Weill-Marchesani syndrome.

Frequency

Weill-Marchesani syndrome appears to be rare; it has an estimated prevalence of 1 in 100,000 people.

Causes

Mutations in the ADAMTS10 and FBN1 genes can cause Weill-Marchesani syndrome. The ADAMTS10 gene provides instructions for making a protein whose function is unknown. This protein is important for normal growth before and after birth, and it appears to be involved in the development of the eyes, heart, and skeleton. Mutations in this gene disrupt the normal development of these structures, which leads to the specific features of Weill-Marchesani syndrome.

A mutation in the FBN1 gene has also been found to cause Weill-Marchesani syndrome. The FBN1 gene provides instructions for making a protein called fibrillin-1. This protein is needed to form threadlike filaments, called microfibrils, that help provide strength and flexibility to connective tissue. The FBN1 mutation responsible for Weill-Marchesani syndrome leads to an unstable version of fibrillin-1. Researchers believe that the unstable protein interferes with the normal assembly of microfibrils, which weakens connective tissue and causes the abnormalities associated with Weill-Marchesani syndrome.
In some people with Weill-Marchesani syndrome, no mutations in \textit{ADAMTS10} or \textit{FBN1} have been found. Researchers are looking for other genetic changes that may be responsible for the disorder in these people.

\textbf{Inheritance Pattern}

Weill-Marchesani syndrome can be inherited in either an autosomal recessive or an autosomal dominant pattern.

When Weill-Marchesani syndrome is caused by mutations in the \textit{ADAMTS10} gene, it has an autosomal recessive pattern of inheritance. Autosomal recessive inheritance means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other cases of Weill-Marchesani syndrome, including those caused by mutations in the \textit{FBN1} gene, have an autosomal dominant pattern of inheritance. Autosomal dominant inheritance means one copy of the altered gene in each cell is sufficient to cause the disorder. In most cases, an affected person inherits the genetic change from one parent with the condition.

\textbf{Other Names for This Condition}

- brachydactyly-spherophakia syndrome
- brachymorphy with spherophakia syndrome
- congenital mesodermal dysmorphodystrophy
- Marchesani syndrome
- Marchesani-Weill Syndrome
- spherophakia-brachymorphyia syndrome
- WMS

\textbf{Diagnosis & Management}

\textbf{Genetic Testing Information}

- What is genetic testing? /primer/testing/genetictesting
Other Diagnosis and Management Resources

- GeneReview: Weill-Marchesani Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1114

Additional Information & Resources

Health Information from MedlinePlus

- Health Topic: Connective Tissue Disorders
  https://medlineplus.gov/connectivetissuedisorders.html
- Health Topic: Eye Diseases
  https://medlineplus.gov/eyediseases.html

Genetic and Rare Diseases Information Center

- Weill-Marchesani syndrome

Additional NIH Resources

- National Eye Institute: Diagram of the Eye
  https://nei.nih.gov/health/eyediagram/
- National Eye Institute: Facts About Glaucoma
  https://nei.nih.gov/health/glaucoma/glaucoma_facts

Educational Resources

- MalaCards: weill-marchesani syndrome
  https://www.malacards.org/card/weill_marchesani_syndrome
- Orphanet: Weill-Marchesani syndrome
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=3449

Patient Support and Advocacy Resources

- Children's Glaucoma Foundation
  https://www.childrensglaucoma.org/
- Glaucoma Research Foundation
  https://www.glaucoma.org/
- Human Growth Foundation
  https://www.hgffound.org/
- Little People of America
  https://www.lpaonline.org/
- Little People UK
  https://littlepeopleuk.org/
• National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/weill-marchesani-syndrome/
• Resource List from the University of Kansas Medical Center: Connective Tissue Disorders
  http://www.kumc.edu/gec/support/connect.html
• The MAGIC Foundation
  https://www.magicfoundation.org/

Clinical Information from GeneReviews
• Weill-Marchesani Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1114

Scientific Articles on PubMed
• PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28weill-marchesani+syndrome%5BTIAB%5D%29+OR+%28marchesani+syndrome%5BTIAB%5D%29+OR+%28spherophakia-brachymorphism%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM
• WEILL-MARCHESANI SYNDROME 1
  http://omim.org/entry/277600
• WEILL-MARCHESANI SYNDROME 2
  http://omim.org/entry/608328

Medical Genetics Database from MedGen
• Weill-Marchesani syndrome
• Weill-Marchesani syndrome 2
• Weill Marchesani Syndrome, Autosomal Recessive
Sources for This Summary


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