Weill-Marchesani Syndrome

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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.

Keywords: genetic conditions

1. Introduction

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.

2. Frequency

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

3. 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 *ADAMTS10* or *FBN1* have been found. Researchers are looking for other genetic changes that may be responsible for the disorder in these people.

3.1 The genes associated with Weill-Marchesani syndrome

- ADAMTS10
- FBN1

4. Inheritance

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 *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 *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.

5. Other Names for This Condition

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

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