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My46 Trait Profile

Marfan syndrome

Marfan syndrome is a genetic condition of the connective tissue that most commonly affects the heart, eye and skeletal systems. It is mainly caused by mutations in the FBN1 gene that makes a protein called fibrillin-1.

Characteristics of Marfan syndrome

Marfan syndrome (MFS) is a genetic condition that affects approximately 1 in 5,000 to 10,000 people. MFS is considered a disorder of the connective tissue. Connective tissue helps provide strength and flexibility to the body. Because connective tissue is found in many different parts of the body, individuals with MFS may show features in many systems of the body. The most commonly affected systems are the heart (cardiovascular), eyes (ophthalmic), and bones (skeletal). Not all features of MFS are evident when a person is young, some may develop with age. Also, not every person with MFS will have the same features, even within a family (variable expressivity).

The most common finding in the heart is dilation (stretching) or aneurysm (ballooning) of the aorta, typically in the part of the aorta closest to the heart (thoracic). The aorta is the large vessel that is responsible for the blood getting from the heart to the rest of the body. Dilation of the aorta can lead to more serious complications including aortic dissection (tearing of the aortic wall) if not monitored. Mitral valve prolapse (floppiness of the mitral valve in the heart) can also be commonly seen.

Approximately 50-80% of people with Marfan syndrome will have dislocation of the lens in the eye (ectopia lentis). Most individuals with MFS will also have nearsightedness (myopia). There may also be other eye findings seen, but these are less common.

Skeletal features of MFS include long arms and legs and individuals with MFS are typically tall and thin. Their arm span is usually longer than their height (increased arm span to height) and their legs are usually longer than their upper body (reduced upper to lower segment ratios). They may also have long, narrow fingers (arachnodactyly), flat feet (pes planus), curvature of the spine (scoliosis or kyphosis) and a chest/sternum bone that either sticks out (pectus carinatum) or curves in (pectus excavatum). Facial features that are suggestive of Marfan syndrome include a long face (dolicocephaly), slightly down-slanting and recessed eyes (enopthalmos), flat cheeks (malar hypoplasia) and a small or recessed chin (micro-retrognathia). Stretch marks (striae) may be present on the skin and individuals may have more flexible joints. Less commonly, collapsed lungs (pneumothoraces) can occur. Intelligence is usually normal in individuals with MFS.

Diagnosis/Testing

MFS can be diagnosed clinically based on a set of established criteria called the Ghent nosology. These criteria look at the manifestations of the heart, eyes and skeletal system. They also consider if an individual has a family history or positive genetic testing for MFS. Usually, a person must have manifestations of two body systems to have a clinical diagnosis of MFS (e.g. aortic dilation and ectopia lentis).

Most individuals with MFS have a change or mutation in a gene called FBN1. The FBN1 gene makes the fibrillin-1 protein that binds to other molecules to form threadlike structures called microfibrils. These microfibrils in turn form elastic fibers, which make up part of the connective tissue.

Management/Surveillance

Management of MFS includes routine ultrasounds of the heart (echocardiograms) and/or other vascular imaging (MRA, CTA, cardiac MRI as indicated). Exercise restrictions and blood-pressure lowering medications are often used to reduce stress on the aorta. When the aorta grows to the point at which it may need surgery, aortic root replacement surgery is indicated to reduce the risk of aortic dissection. Ocular management includes routine ophthalmological evaluation by slit lamp exam with dilated eyes to monitor for lens dislocation and nearsightedness. Skeletal features are often followed by an Orthopedics physician, and surgery or bracing may be indicated to correct scoliosis or chest wall deformities in some cases.

Mode of inheritance

MFS is inherited in an autosomal dominant pattern. This means inheriting one FBN1 mutation is enough for an individual to be affected and show signs of MFS. The mutation can be inherited from an affected parent or it can occur brand new (de novo) in an affected child. It is estimated that 25% of individuals with MFS have a de novo mutation.

Risk to family members

The risk to family members depends on whether or not the individual with MFS has a parent affected with MFS. If a parent also has MFS, the risk of having a child with MFS is 50% with each pregnancy. If a parent does not have MFS, the risk of other siblings being affected is very low.

Special considerations

None

Resources

National Marfan Foundation
http://www.marfan.org/marfan/
Genetics Home Reference: Marfan Syndrome
http://ghr.nlm.nih.gov/gene/FBN1

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