X-linked cardiac valvular dysplasia

Description

X-linked cardiac valvular dysplasia is a condition characterized by the abnormal development (dysplasia) of heart (cardiac) valves. The normal heart has four valves, two on the left side of the heart and two on the right side, that allow blood to move through the heart and prevent blood from flowing backward. In X-linked cardiac valvular dysplasia, one or more of the four heart valves is thickened and cannot open and close completely when the heart beats and pumps blood. These malformed valves can cause abnormal blood flow and an irregular heart sound during a heartbeat (heart murmur).

The signs and symptoms of X-linked cardiac valvular dysplasia vary greatly among affected individuals. Some people have no health problems, while in others blood can leak through the thickened and partially closed valves. This valve leakage (regurgitation) typically affects the mitral valve, which connects the two left chambers of the heart, or the aortic valve, which regulates blood flow from the heart into the large artery called the aorta. Valve regurgitation forces the heart to pump harder to move blood through the heart. As a result, affected individuals may develop chest pains, shortness of breath, or lightheadedness.

In X-linked cardiac valvular dysplasia, the mitral or aortic valve can also be prolapsed, which means that the valve is weak or floppy. Valve prolapse further prevents the thickened valve from closing properly and can lead to valve regurgitation. Other rare complications of X-linked cardiac valvular dysplasia include inflammation of the inner lining of the heart (endocarditis), abnormal blood clots, or sudden death.

X-linked cardiac valvular dysplasia can be diagnosed anytime from birth (in some cases prenatally) to late adulthood but is typically diagnosed in early to mid-adulthood because valve malformation is often a slow process. This condition affects males more often and more severely than females.

Frequency

The prevalence of X-linked cardiac valvular dysplasia is unknown. Approximately 3 percent of the population has a heart valve defect, only a small fraction of which are associated with X-linked cardiac valvular dysplasia.

Causes

X-linked cardiac valvular dysplasia is caused by mutations in the *FLNA* gene. This gene provides instructions for producing the protein filamin A, which helps build cells' extensive internal network of protein filaments called the cytoskeleton. The cytoskeleton gives structure to cells and allows them the flexibility to change shape. Filamin A primarily attaches (binds) to another protein called actin and helps it form the branching network of filaments that make up the cytoskeleton.

Filamin A also plays a role in the organization of the extracellular matrix, which is the lattice of proteins and other molecules outside the cell. Filamin A helps anchor cells to the extracellular matrix to ensure that cells are correctly positioned and signals can be exchanged between the cell and the extracellular matrix. Proper development of heart valves requires precise organization of cells within the extracellular matrix.

FLNA gene mutations that cause X-linked cardiac valvular dysplasia decrease the protein's ability to bind to actin and other proteins within the cell. As a result, the cell cytoskeleton is weakened and the extracellular matrix is disorganized. The cells' decreased ability to change shape impairs the valve's ability to open and close when the heart pumps blood. In addition, it appears that excess proteins are produced in the abnormal extracellular matrix, causing the valves to become thickened and further impairing their ability to open and close normally.

Filamin A is important in cells that make up many tissues in the body; it is unclear why the heart valves are the only tissue affected by the *FLNA* gene mutations that cause X-linked cardiac valvular dysplasia.

Learn more about the gene associated with X-linked cardiac valvular dysplasia

- FLNA

Inheritance

This condition is inherited in an X-linked pattern. A condition is considered X-linked if the mutated gene that causes the disorder is located on the X chromosome, one of the two sex chromosomes in each cell. In males, who have only one X chromosome, a mutation in the only copy of the gene in each cell is sufficient to cause the condition. In females, who have two copies of the X chromosome, one altered copy of the gene in each cell can lead to less severe features of the condition or may cause no signs or symptoms at all. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

Other Names for This Condition

- Congenital valvular heart disease
- CVD1
- Filamin-A-associated myxomatous mitral valve disease

- Filamin-A-related myxomatous mitral valve dystrophy
- X-linked myxomatous valvular dystrophy
- XMVD

Additional Information & Resources

Genetic and Rare Diseases Information Center

- FLNA-related X-linked myxomatous valvular dysplasia (https://rarediseases.info.nih.gov/diseases/1096/index)

Patient Support and Advocacy Resources

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

Catalog of Genes and Diseases from OMIM

- CARDIAC VALVULAR DYSPLASIA, X-LINKED; CVDPX (https://omim.org/entry/314400)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28filamin+A%5BALL%5D%29+AND+%28myxomatous+valvular+dystrophy%5BALL%5D%29+OR+%28myxomatous+mitral+valve+disease%5BALL%5D%29+OR+%28cardiac+valvular+dysplasia%5BALL%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

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Last updated March 1, 2018