Ankyrin-B syndrome

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Ankyrin-B syndrome is associated with a variety of heart problems related to disruption of the heart's normal rhythm (arrhythmia). Heart rhythm is controlled by electrical signals that move through the heart in a highly coordinated way. In ankyrin-B syndrome, disruption of different steps of electrical signaling can lead to arrhythmia, and the resulting heart problems vary among affected individuals.

genetic conditions

1. Introduction

Individuals with ankyrin-B syndrome may have problems with the sinoatrial (SA) node, which generates the electrical impulses that start each heartbeat. If the SA node is not functioning properly, the heartbeat can be too slow (bradycardia). In a small number of people with ankyrin-B syndrome, the heart takes longer than usual to recharge between beats, which is known as a prolonged QT interval (long QT). Some affected individuals have impaired progression (conduction) of electrical impulses between the chambers of the heart, which can cause a problem called heart block. Other heart problems that occur in ankyrin-B syndrome include irregular and uncoordinated electrical activity in the heart's upper chambers (atrial fibrillation) or lower chambers (ventricular fibrillation) and an abnormality called catecholaminergic polymorphic ventricular tachycardia (CPVT), in which an increase in the heart rate can trigger an abnormally fast and irregular heartbeat called ventricular tachycardia. In people with ankyrin-B syndrome, arrhythmia can lead to fainting (syncope) or cardiac arrest and sudden death.

When associated with a prolonged QT interval, the condition is sometimes classified as long QT syndrome 4. However, because additional heart problems can result from changes in the same gene, long QT syndrome 4 is usually considered part of ankyrin-B syndrome.

2. Frequency

Ankyrin-B syndrome is a rare disorder. Its prevalence is unknown.

3. Causes

Ankyrin-B syndrome is caused by mutations in the *ANK2* gene, which provides instructions for making a protein called ankyrin-B. This protein is active in many cell types, including heart (cardiac) muscle cells. The ankyrin-B protein inserts certain structures called ion channels into their proper locations in the cell membrane. Ion channels

are complexes of proteins that transport charged atoms (ions) across cell membranes. In the heart, the flow of ions (such as sodium, potassium, and calcium) through ion channels generates the electrical signals that control the heartbeat and maintain a normal heart rhythm.

Mutations in the *ANK2* gene lead to production of an altered ankyrin-B protein that cannot target ion channels to their correct locations in cardiac muscle cells. The loss of functional ion channels in the heart disrupts the normal flow of ions, which alters the heart's normal rhythm and causes the heart problems associated with ankyrin-B syndrome.

Not everyone with an *ANK2* gene mutation has heart problems related to ankyrin-B syndrome. Researchers speculate that other genes or environmental factors may play a role in development of the condition.

3.1. The gene associated with Ankyrin-B syndrome

- ANK2

4. Inheritance

Ankyrin-B syndrome is inherited in an autosomal dominant pattern, which means one copy of the altered *ANK2* gene in each cell is sufficient to cause the disorder. In most cases, an affected person has one parent with the condition.

Some people who have an altered *ANK2* gene never develop heart problems, a situation known as reduced penetrance.

5. Other Names for This Condition

- cardiac arrhythmia, ankyrin-B-related

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