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My46 Trait Profile

Char syndrome

Char syndrome is a rare genetic condition with characteristic facial features and birth defects of the heart and hands. It is caused by mutations in the TFAP2B gene which makes a protein called transcription factor AP-2 beta.

Characteristics of Char syndrome

Char syndrome is a rare genetic condition that is classically characterized by three findings: typical facial features, a congenital heart defect, and abnormalities of the fifth finger (pinkie). The facial features commonly seen include a flattened forehead and cheekbones. The tip and bridge of the nose are often flattened as well. The forehead and tip of the nose may also be broad. The eyes may be wide-set and eyelids can be droopy (ptosis). The eyes may also down slanting. The distance between the nose and upper lip (the philtrum) can be shorter than usual, causing the mouth to look triangular. The lips are often thick.

The most common heart defect seen in individuals with Char syndrome is a patent ductus arteriosus (PDA). The ductus arteriosus is a blood vessel that is part of the circulatory system during fetal life. It connects two major arteries, the pulmonary artery and the aorta. The pulmonary artery is connected to the right side of the heart and allows blood to flow to the lungs to receive oxygen. The aorta is connected to the left side of the heart and supplies oxygen-rich blood to the body. The ductus arteriosus is needed to bypass the lungs, which are filled with fluid during pregnancy. Once a baby is born, the ductus arteriosus typically closes on its own. If the ductus arteriosus does not close after birth it is said to be patent (open). Failure of the ductus arteriosus to close after birth can cause the heart and lungs to work harder than normal, by allowing the oxygen-low blood from the right side of the heart to mix with the oxygen-rich blood from the left side of the heart. Less commonly, other types of heart defects have been reported in individuals with Char syndrome.

The hand abnormalities seen in individuals with Char syndrome most commonly include either shortening (hypoplasia) or absence (aplasia) of the middle bone in the fifth finger. The fifth finger may also be bent inward (clinodactyly). Less commonly reported features of Char syndrome include extra nipples (polythelia), missing teeth (hypodontia), extra toes or toes that are fused, hearing and vision problems or problems while sleeping, and developmental delay.

Also, not every person with Char syndrome will have the same features, even within a family (variable expressivity). For example, some people may only have a PDA, while others may only have facial features and hand abnormalities.

Diagnosis/Testing

Approximately 50% of individuals with clinical features of Char syndrome have a change or mutation in the TFAP2B gene which makes a transcription factor protein. Transcription factors are important in helping regulate the activity of other genes. They do this by attaching to other genes, which can turn them on or off. The TFAP2B encoded transcription factor helps to control the activity of genes that are responsible for how the body develops before birth. Genes that control the development of the heart, structures of the face and hands are most affected, leading to the signs and symptoms of Char syndrome. Sometimes, individuals with certain TFAP2B mutations are more likely to have specific features of the condition. This is called genotype/phenotype correlation. Some alterations have been associated with milder facial features and no hand abnormalities, but a higher risk of PDA and other congenital heart defects.

Approximately 50% of individuals with clinical features of Char syndrome do not have a mutation in the TFAP2B

gene. This suggests that mutations in other genes might cause Char syndrome.

Management/Surveillance

Management of Char syndrome is mainly aimed at preventing complications from a PDA. Sometimes medications are given to help close a PDA. Some PDAs may require surgical closure during infancy by a procedure involving a heart catheterization (putting a thin tube into the heart). Once treated, infants typically do well. Although other problems are less common, hearing and vision should be evaluated, as should development, during infancy and childhood.

Mode of inheritance

Char syndrome is inherited in an autosomal dominant pattern. This means inheriting one mutation is enough for an individual to be affected and show signs of Char syndrome. A mutation can be inherited from a parent or it can occur brand new (de novo) in a person. Because Char syndrome is so rare, the percentage of people that have a de novo mutation is not known. The majority of individuals with Char syndrome reported have an affected parent.

Risk to family members

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

Special considerations

None

Resources

Little Hearts, Inc.
https://www.littlehearts.org/Default.asp
Congenital Heart Information Network
http://tchin.org
Genetics Home Reference: Char syndrome
http://ghr.nlm.nih.gov/condition/char-syndrome

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