Published on *My46* (https://www.my46.org) 10/16/2021
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My46 Trait Profile

Costello syndrome

Costello syndrome is a genetic condition with characteristic facial features and birth defects. It is caused by mutations in the HRAS gene which makes the protein called H-Ras.

Characteristics of Costello syndrome

Costello syndrome is a rare genetic condition with characteristic facial features such as macrocephaly (i.e., large head size), curly hair, a high forehead, short nose, full cheeks, a large mouth, thick lips, and multiple congenital anomalies (i.e., birth defects) such as heart defects (e.g., pulmonic stenosis: narrowing of the narrowing of the artery that carries blood from the heart to the lungs) and skeletal abnormalities (e.g., scoliosis: curving of the spine). Not all heart defects in this syndrome are present at birth; hypertrophic cardiomyopathy (i.e., a heart condition where the heart becomes thicker, making it more difficult for it to pump blood to the rest of the body) may develop later in infancy or in early childhood and can be rapidly progressive. Older individuals with Costello syndrome may develop additional heart complications such as arrhythmias (i.e., an irregular heart beat). Other characteristic features include facial papillomas (i.e., small skin growths), loose skin, deep creases in the palms of the hands and soles of the feet, and ulnar deviation of the fingers and wrist (i.e., turning towards the pinky finger). Most individuals with Costello syndrome have short stature, hypotonia (i.e., low muscle tone), and severe failure to thrive. Individuals with Costello syndrome are at risk for developing certain cancers such as rhabdomyosarcoma (i.e., a cancerous tumor of the skeletal muscles), neuroblastoma (i.e., a cancerous tumor of nerve tissue), and bladder cancer. Varying degrees of developmental delay and/or intellectual disability are seen in all individuals with Costello syndrome.

Diagnosis/Testing

Most individuals with Costello syndrome have a change or mutation in the HRAS gene. This gene makes the H-Ras protein which is involved in a complex signaling pathway called the “RAS-MAPK pathway.” This pathway is important for the proper formation of many different types of tissue during human development. A mutation in this gene disrupts this signaling pathway.

Management/Surveillance

Management and surveillance of individuals with Costello syndrome often includes regular physical exams, eye exams, hearing evaluations, neurological evaluations, head imaging, ultrasounds of the heart, and bone density tests. In addition, developmental evaluations and educational services such as speech, occupational, and physical therapies are highly recommended. Because of the increased risk for developing certain cancers, regular abdominal ultrasounds and urine tests are also recommended.

Mode of inheritance

Costello 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 Costello syndrome. Instead of being inherited from an affected parent, the mutation most often occurs brand new (de novo) in an affected child.

Risk to family members

The risk to family members depends on whether or not the individual with Costello syndrome has a parent affected with Costello syndrome. Since the overwhelming majority of individuals with Costello syndrome do not have an affected parent, the risk of future pregnancies being affected is very low.

Special considerations

None

Resources

CostelloKids
http://costellokids.com/
Costello syndrome: A booklet by parents for parents
http://costellokids.com/sites/default/files/CS%20booklet%208.5x11.pdf
Genetics Home Reference: Costello syndrome
http://ghr.nlm.nih.gov/condition/costello-syndrome

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Created: 01/2013 **Created by:** Seema Jamal, MSc, LCGC
Updated: mm/yyyy