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My46 Trait Profile

Wolf-Hirschhorn syndrome

Other Names: 4p- syndrome, Monosomy 4p, 4p deletion syndrome, Pitt-Rogers-Danks syndrome

Wolf-Hirschhorn syndrome results from a deletion of genetic material on one of the short arms of chromosome 4. This deletion results in the loss of several genes.

Characteristics of Wolf-Hirschhorn syndrome

Wolf-Hirschhorn syndrome (WHS) is a condition that affects many different parts of the body. While each individual with WHS is unique, there are some common features which are seen in most individuals with the condition. Individuals with WHS typically have slow growth, both before and after birth, low muscle tone (hypotonia), mild to severe developmental delay, and central nervous system problems such as seizures. The most defining characteristic of WHS, however, is the combination of unique facial features. These include large wide-spaced eyes (hypertelorism), a prominent glabella (the area of the forehead between the eyebrows and above the nose), a small chin (micrognathia), and a short philtrum (the area between the nose and upper lip). Together these facial features are said to look like a Greek warrior helmet.

Individuals with WHS often have birth defects. The most common birth defects are heart defects, which are usually simple such as ventricular septal defect (i.e., a hole between the lower two chambers of the heart), cleft lip and cleft palate, and club foot. Other features which are commonly seen in individuals with WHS are feeding difficulties (such as difficulty with sucking, swallowing and acid reflux), dental problems (such as delayed tooth development), difficulty fighting infection, hearing problems, and vision problems.

While developmental delays and intellectual disability is a common feature, most individuals with WHS have excellent social skills and want to interact with others. Their development continues to progress, often achieving new cognitive and motor skills throughout their life.

Diagnosis/Testing

Diagnosis of WHS is usually made in childhood after referral to a specialist for characteristic facial features, slow growth, developmental delay, and/or seizures. When WHS is suspected after clinical evaluation, the diagnosis is confirmed by genetic testing.

WHS is caused by a deletion (missing piece) of the Wolf-Hirschhorn critical region (WHSCR) within chromosome 4p16.3. A microarray (also known as an oligoarray, SNP array or arrayCGH) is a blood test which can simultaneously evaluate the cells for small pieces of genetic material that may be missing or extra on each chromosome (the packages of genetic material). A blood test known as FISH (fluorescence in situ hybridization) involves attaching fluorescent probes to the specific area of interest and is frequently used for testing family members of affected individuals.

Management/Surveillance

Since many features of WHS can be difficult to detect, all individuals with WHS should have a heart exam, regular hearing evaluation, and an eye exam. Evaluation of seizures is very important. Cognition, language, motor development, and social skills should be evaluated as each individual's development is unique.

Management of WHS is specific to each individual, but often involves many medical specialists. Feeding problems

may require interventions such as placement of a feeding tube. Skeletal anomalies, such as club foot and scoliosis, should be addressed, and treatment with surgery and/or physical therapy should be considered. Seizures can often be controlled with certain medications. Occupational, physical, and developmental therapy can assist with motor skills and social skills.

Mode of inheritance

WHS is inherited in an autosomal dominant pattern. This means inheriting one 4p16.3 microdeletion is enough for an individual to be affected and show signs of WHS. In approximately 55% of cases, the deletion occurs brand new (de novo) in an affected child. The remaining individuals with WHS have an unbalanced chromosome translocation. This means they have both a 4p deletion and partial duplication (extra piece) of another chromosome. Some unbalanced translocations are inherited from a parent with a balanced translocation (where part of one chromosome is attached to another chromosome, but no genetic material is missing).

Risk to family members

The risk to family members depends on whether or not the individual with WHS has a deletion that is part of an unbalanced translocation. If a parent carries a balanced translocation, the risk of recurrence to future offspring is increased. The level of risk depends on the specific chromosome rearrangement the parent carries. The family members of a parent with a balanced chromosome translocation have an increased risk of also carrying the translocation. If a parent does not carry a balanced translocation, the risk of other siblings being affected is very low.

Special considerations

None

Resources

Genetic Home Reference: Wolf-Hirschhorn syndrome
http://ghr.nlm.nih.gov/condition/wolf-hirschhorn-syndrome
4p- support group
http://4p-supportgroup.org
WolfHirschhorn.org
http://wolfhirschhorn.org/

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