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My46 Trait Profile

Miller syndrome

Other Names: Genne-Wiedemann syndrome, postaxial acrofacial dysostosis (POADS), Wildervanck-Smith syndrome

Miller syndrome is a rare genetic condition characterized by birth defects affecting the head, face, arms, and legs. It is caused by mutations in the DHODH gene which makes the dihydroorotate dehydrogenase enzyme.

Characteristics of Miller syndrome

Miller syndrome is a rare condition occurring in less than one in a million newborns. It primarily affects development of the face and limbs. Individuals with Miller syndrome are born with underdeveloped cheekbones, a very small lower jaw, and frequently a cleft palate (opening in the roof of the mouth) or cleft lip (split in the upper lip). These developmental abnormalities can result in feeding and breathing problems. Affected individuals also have eyes that slant downwards and inverted eyelids that expose their inner surface. Many can have a notch or key-hole-like opening in the lower eyelid (eyelid coloboma). Other common features are small, cup shaped ears and extra nipples. There can additionally be conductive hearing loss due to a middle ear deformity.

Various bone abnormalities, particularly involving the arms and legs, are often see in individuals with Miller syndrome. The most frequently occurring finding is the absence of the fifth (pinky) finger or toe. There may also be syndactyly or webbed fingers or toes and abnormally formed bones of the arms, legs, spine and ribs. Less commonly, individuals can have problems with the heart, kidneys, genitals and gastrointestinal tract. There are no intellectual disabilities or developmental delays related to Miller syndrome; however, speech may be impaired due to hearing deficits.

Diagnosis/Testing

Most individuals with Miller syndrome have changes or mutations in a gene called DHODH. This gene makes the dihydroorotate dehydrogenase enzyme. This enzyme is involved in making the building blocks of DNA. It is not entirely understood why and how mutations in the DHODH gene cause the features seen in Miller syndrome.

Management/Surveillance

Treatment for Miller syndrome may include surgery to insert breathing and feeding tubes for infants with deformities of the jaw and palate. Due to misshapen ears, ear tubes may also be needed. In order to correct eye and jaw deformities, multiple plastic surgeries may be necessary. For limb abnormalities, physical therapy may be necessary for assistance with mobility. If cleft lip or palate is present, surgical intervention and speech therapy are typically indicated.

Mode of inheritance

Miller syndrome is inherited in an autosomal recessive pattern. This means that an individual has to inherit two DHODH mutations (i.e., one from each parent) to be affected with Miller syndrome. If both parents are carriers of a DHODH mutation, they have a 1 in 4 (25%) chance with each pregnancy of having a child with Miller syndrome.

Risk to family members

Parents of a child with Miller syndrome are carriers of Miller syndrome. If a sibling of a child with Miller syndrome is unaffected, he/she has a 2 in 3 (66%) chance of being a carrier of Miller syndrome.

Special considerations

None

Resources

Genetics Home Reference: Miller syndrome
http://ghr.nlm.nih.gov/condition/miller-syndrome
Foundation for Nager and Miller syndromes
http://www.fnms.net/category/345/the-syndromes
National Organization for Rare Disorders: Miller syndrome
http://www.rarediseases.org/rare-disease-information/rare-diseases/byID/891/viewFullReport
The National Craniofacial Association: Miller syndrome
http://www.faces-cranio.org/Disord/Miller.htm

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