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My46 Trait Profile

Menkes syndrome

Menkes syndrome is a metabolic disorder caused by low levels of copper in the blood that can lead to progressive intellectual disability, bone abnormalities, loose skin, and coarse, kinky hair.

Characteristics of Menkes syndrome

Individuals with Menkes syndrome are typically healthy at birth. During infancy, they may have weak muscles (i.e. hypotonia) and feeding difficulties. One of the first clues that a child has Menkes syndrome may be the presence of sparse, light colored hair, which is often described as “kinky.” The face may look a little different and have pale skin, small chin, pudgy cheeks, and a large forehead. Babies with Menkes syndrome typically develop normally until 3 to 5 months of age, when they start to show significant developmental delay, and begin to lose developmental skills they once were able to perform, such as sitting. Developmental problems are progressive (i.e. worsen over time) and result in significant intellectual disability. Infants with Menkes syndrome develop seizures (i.e. abnormal electrical activity in the brain), and may have abnormalities in the structure of the brain.

Children with Menkes syndrome can also have bone changes, such as a caved in chest (i.e. pectus excavatum) or a curved spine (i.e. scoliosis). They may have flexible joints, and are at risk for frequent bone fractures. Menkes syndrome also causes the skin on the body to be loose and wrinkly, a condition called cutis laxa. Umbilical hernias are also common among children with Menkes syndrome.

Symptoms of Menkes syndrome are caused by the inability to transport copper from cells to tissues. Seizures and intellectual disability are related to low levels of copper in the brain. Due to the progressive nature of Menkes syndrome, children with this condition do not typically survive past early childhood. However, there is a wide spectrum of severity, and some individuals live longer and respond to treatment (described below).

Diagnosis/Testing

If a healthcare provider suspects that a child may have Menkes syndrome based on symptoms and appearance, he/she may draw blood to measure the amount of copper and ceruloplasmin (a protein that interacts with copper) in the blood. Individuals with MS have low levels of blood copper and ceruloplasmin. However, some people without Menkes syndrome have low levels as well, so this test by itself cannot make the diagnosis of Menkes syndrome. In order to confirm a diagnosis of Menkes syndrome, genetic testing is performed. Menkes is caused by genetic changes or mutationsin a gene called ATP7A.

Management/Surveillance

Management of Menkes syndrome is mainly symptomatic, meaning that each symptom is treated individually when it occurs. For example, many individuals take medication for their seizures. Surgery can be performed for children who have hernias, or broken bones.

One treatment that may be effective in some individuals with Menkes syndrome is copper injections. Some people with Menkes syndrome who have received copper injections regularly have experienced improved intellectual ability, fewer seizures, and have longer lives. Not all people with Menkes syndrome improve with copper injections.

Mode of inheritance

Menkes syndrome is inherited in an X-linked recessive pattern. The ATP7A gene mutaitons causing this type of

inheritance is found on the X-chromosome. An X-linked recessive pattern means that in females, both copies of the ATP7A gene (i.e., one on each X chromosome) must have a mutation, whereas in males, only one copy of the ATP7A gene must have a mutation to be affected. A female with a mutation in one copy of the ATP7A gene on the X chromosome is said to be a carrier for an X-linked condition, and is typically not affected.

Risk to family members

If a father is affected with Menkes syndrome, his daughters will be carriers of Menkes syndrome and his sons will be unaffected. If a mother is a carrier of Menkes syndrome, each daughter has a 1 in 2 chance (i.e., 50%) of being a carrier and each son has a 1 in 2 chance (i.e., 50%) of being affected with Menkes syndrome.

Special considerations

Occipital horn syndrome (OHS) is a genetic disorder that is also caused by mutations in the ATP7A gene and is considered to be a very mild form of Menkes syndrome. It is very similar, but does not cause significant intellectual disability or seizures.

Resources

The Menkes Foundation
http://themenkesfoundation.org/
Genetics Home Reference: Menkes syndrome
http://ghr.nlm.nih.gov/condition/menkes-syndrome

References

Kaler SG. (2011).ATP7A-related copper transport diseases – emerging concepts and future trends.” Nature Reviews: Neurology 7: 15-29.
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