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Walker-Warburg syndrome, *FKTN*-related

What is Walker-Warburg syndrome?

Walker-Warburg syndrome is an inherited disease characterized by muscle, brain, and eye abnormalities. Individuals with Walker-Warburg syndrome have defects in the protein fukutin, which adds chains of sugars to proteins involved in connecting the internal and external structure of cells, in protecting muscle fibers, and in the development of the nervous system. Symptoms are due to abnormal cell structure and function, particularly in the brain, eyes, and muscles.[1] Walker-Warburg syndrome is the most severe of a group of inherited muscle disorders known as alpha-dystroglycanopathies, and is also known as muscular dystrophy-dystroglycanopathy, type A4.[2]

What are the symptoms of Walker-Warburg syndrome and what treatment is available?

Walker-Warburg syndrome is a disease that is present at birth, and symptoms progress throughout an individual's life. Signs and symptoms may include:[3]

- Hypotonia (low muscle tone)
- Muscle weakness
- Eye abnormalities that can cause blindness
- Brain abnormalities, including cobblestone lissencephaly
- Hydrocephalus (fluid in the brain)
- Mental retardation
- Seizures

There is no cure for Walker-Warburg syndrome. Treatment includes supportive care for symptoms, such as medications for seizures, feeding tubes, and surgical intervention for hydrocephalus. Most individuals do not live beyond three years of age.[3]

How is Walker-Warburg syndrome inherited?

Walker-Warburg syndrome is an autosomal recessive disease caused by mutations in one of at least six genes, including the *FKTN* gene.[5] An individual who inherits one *FKTN* gene mutation is a carrier and is not expected to have related health problems. An individual who inherits two *FKTN* mutations, one from each parent, is expected to be affected with a dystroglycanopathy, such as Walker-Warburg syndrome or Fukuyama congenital muscular dystrophy.[4]

If both members of a couple are carriers of a mutation in the same gene, the risk of having an affected child is 25% in each pregnancy; therefore, it is especially important that the reproductive partner of a carrier be offered testing.

Who is at risk for Walker-Warburg syndrome, *FKTN*-related?

Walker-Warburg syndrome can occur in individuals of all races and ethnicities. In the Ashkenazi Jewish (Eastern European) population, the carrier frequency is estimated to be 1 in 79.[6]

Having a relative who is a carrier or is affected can increase an individual's risk to be a carrier. Consultation with a genetics health professional may be helpful in determining carrier risk and appropriate testing.

What does a positive test result mean?

If a gene mutation is identified, an individual should speak to a physician or genetics health professional about the implications of the result and appropriate testing for the reproductive partner and at-risk family members.

What does a negative test result mean?

A negative result reduces, but does not eliminate, the possibility that an individual carries a gene mutation. The likelihood of being a carrier is also influenced by family history, medical symptoms, and other relevant test results.

Where can I get more information?

Cure CMD: www.curecmd.org

Muscular Dystrophy Association - USA (MDA): www.mda.org

Congenital Muscular Dystrophy International Registry (CMDIR): www.cmdir.org

References

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