Inheritest® CARRIER SCREEN

Alpha-mannosidosis

What is alpha-mannosidosis?

Alpha-mannosidosis is an inherited disease characterized by developmental delays, facial and skeletal abnormalities, hearing loss, and immune deficiency.[1] It is caused by abnormalities in the enzyme alpha-mannosidase, which breaks down small sugar molecules called oligosaccharides. Symptoms associated with alpha-mannosidosis are due to the toxic build-up of oligosaccharides and the progressive destruction of cells, particularly in the central nervous system.[2]

What are the symptoms of alpha-mannosidosis and what treatment is available?

Alpha-mannosidosis is a disease that varies in severity and age at presentation, even within families. Symptoms may include:[1,2]

- Progressive myopathy (muscle weakness and pain)
- Ataxia (difficulty controlling movements)
- Developmental delays
- Intellectual disability
- Hearing loss
- Distinctive facial characteristics (large head, prominent forehead, low hairline, large ears, protruding jaw, and widely spaced teeth)
- Hydrocephalus
- Joint and bone abnormalities (types 2 and 3)
- Frequent infections
- Psychiatric disease (confusion, anxiety, depression, hallucinations)

Three types of alpha-mannosidosis have been described. Most individuals experience symptoms before age 10, with a slow progression (type 2). Some individuals experience milder symptoms after age 10, with no skeletal abnormalities and even slower progression (type 1). A severe form may also occur with onset during infancy, a rapid progression, and early death (type 3).[1]

There is no cure for alpha-mannosidosis. Many individuals live more than 50 years (types 1 & 2); however, long-term prognosis is poor with the majority of individuals becoming wheelchair-dependent.[1] Treatment is supportive and includes antibiotics to fight infections, hearing aids, and surgery if needed for bone abnormalities.[3] Bone marrow transplant may be beneficial in some individuals if alpha-mannosidosis is diagnosed before the onset of neurological symptoms.[3]

How is alpha-mannosidosis inherited?

Alpha-mannosidosis is an autosomal recessive disease caused by mutations in the *MAN2B1* gene.[2] An individual who inherits one copy of a *MAN2B1* gene mutation is a carrier and is not expected to have health related problems. An individual who inherits two *MAN2B1* mutations, one from each parent, is expected to be affected with alpha-mannosidosis.

If both members of a couple are carriers, the risk for 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 alpha-mannosidosis?

Alpha-mannosidosis can occur in individuals of all races and ethnicities. The incidence of alpha-mannosidosis in the Caucasian population is approximately 1 in 500,000, with a calculated carrier frequency of approximately 1 in 350.[2]

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

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What does a positive test result mean?

If a gene mutation is identified, an individual should speak to a physician or a 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 medical tests.

Where can I get more information?

ISMRD: The International Advocate for Glycoprotein Storage Diseases: http://www.ismrd.org/the_diseases/alpha_mannosidosis

CLIMB: Children Living with Inherited Metabolic diseases: http://www.climb.org.uk/

References

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3. Malm D, Nilssen O. Alpha-Mannosidosis. *GeneReviews* Available at: http://www.ncbi.nlm.nih.gov/books/NBK1396/. Accessed March 3, 2012.