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Leigh syndrome

What is Leigh syndrome?

Leigh syndrome is an inherited progressive neurodegenerative disease characterized by developmental delays or regression, low muscle tone, neuropathy, and severe episodes of illness that can lead to early death.[1,2] Individuals with Leigh syndrome have defects in one of many proteins involved in the mitochondrial respiratory chain complexes that produce energy in cells.[1] These protein defects cause lesions in tissues that require large amounts of energy, including the brainstem, thalamus, basal ganglia, cerebellum, and spinal cord.[1] Clinical symptoms depend on which areas of the central nervous system are involved.[1,2] Leigh syndrome is also known as subacute necrotizing encephalomyelopathy.[3]

What are the symptoms of Leigh syndrome and what treatment is available?

Leigh syndrome is a disease that varies in age at onset and rate of progression. Signs of Leigh syndrome can be seen before birth, but are usually noticed soon after birth. Signs and symptoms may include:[2,3,4]

- Hypotonia (low muscle tone)
- Intellectual and physical developmental delay and regression
- Digestive problems and failure to thrive
- Cerebellar ataxia (difficulty coordinating movements)
- Peripheral neuropathy (disease affecting nerves)
- Hypertrophic cardiomyopathy
- Breathing problems, leading to respiratory failure
- Metabolic or neurological crisis (serious episode of illness) often triggered by an infection

During a crisis, symptoms can progress to respiratory problems, seizures, coma, and possibly death.

There is no cure for Leigh syndrome. Treatment is supportive. Approximately 50% of affected individuals die by three years of age, although some patients may survive beyond childhood.[4]

How is Leigh Syndrome inherited?

Autosomal recessive Leigh syndrome is caused by mutations in at least 36 different genes,[3] including *FOXRED1, NDUFAF2, NDUFS4, NDUFS7, NDUFV1, COX15, SURF1* and *LRPPRC.* The French Canadian type of Leigh syndrome is caused by mutations in *LRPPRC*.[5] An individual who has one mutation in any of these genes is a carrier and is not expected to have related health problems. An individual who has two mutations in one of these genes, one mutation from each parent, is expected to be affected with autosomal recessive Leigh syndrome. For example, a child with two *SURF1* mutations is expected to be affected, but a child with one *SURF1* mutation and one *LRPPRC* mutation is a carrier.

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 Leigh Syndrome?

Autosomal recessive Leigh syndrome can occur in individuals of all races and ethnicities and has a worldwide carrier frequency of approximately 1 in 100.[4] Leigh syndrome, French Canadian type, is most common in individuals of French Canadian ancestry, specifically those from the Saguenay-Lac-Saint-Jean region of Quebec, and it has a carrier frequency estimated at 1 in 23 and an estimated incidence of 1 in 2063 live births.[6]

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 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?

Genetics Home Reference: http://ghr.nlm.nih.gov/condition/leigh-syndrome

National Institutes of Neurological Disorders and Stroke: http://www.ninds.nih.gov/disorders/leighsdisease/leighsdisease.htm

National Organization for Rare Disorders (NORD): http://rarediseases.org/rare-diseases/leigh-syndrome/

References

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