Leigh Syndrome

classical Leigh syndrome, Leigh necrotizing encephalopathy, Leigh's disease, necrotizing encephalomyelopathy of Leigh's, SNE, subacute necrotizing encephalopathy

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Leigh syndrome is a rare mitochondrial condition where the body is not able to use oxygen to change energy from food into a form of energy it can use the way that it should. Mitochondria are parts of a cell that help turn the energy we get from food into energy that the body can use. They are also important in the communication between body parts and creating other materials the body needs. Mitochondrial conditions can cause a variety of signs and symptoms in many parts of the body, particularly those that use a lot of energy like muscles and the brain.

Genetics

Leigh syndrome is a genetic condition, meaning it is passed down or inherited in a family. Leigh syndrome can be caused by changes in over 75 different genes. 80% of the time, the genetic change is in the nuclear DNA, or set of DNA present in every cell of the body and inherited from both parents. Leigh syndrome can also be caused by changes in the mitochondrial genome (mtDNA) or set of DNA contained in the mitochondria of a cell. Both males and females can inherit Leigh syndrome.

Frequency

Leigh syndrome is thought to affect approximately 1 in every 40,000 newborns. Leigh syndrome is more common in some populations like the Saguenay Lac-Saint-Jean region of Quebec, Canada or the Faroe Islands, a self-governing part of the Kingdom of Denmark.

Signs and Symptoms

The signs and symptoms of Leigh syndrome are related to degeneration of the central nervous system including the brain, spinal cord and optic nerve, which is the nerve that talks to the eyes. Symptoms typically appear when an individual is born but can also present later in childhood. The exact features, onset, and severity can vary widely among people with this condition, even among members of the same family. Always check with your provider if new symptoms appear or you are concerned.

Signs and symptoms may include:

- Delay in meeting typical developmental milestones
- Loss of thought and motor skills (psychomotor regression)
- Loss of appetite and trouble gaining/keeping weight or growing (failure to thrive)
- Muscle weakness and low muscle tone (hypotonia)
- Loss Of movement control and balance (dystonia and ataxia)
- Tremors
- Muscle spasms (spasticity)
- Loss of sensation (peripheral neuropathy)
- Vomiting
- Irritability
- Continual crying
- Seizures
- Episodes of high lactate in the blood called lactic acidosis
- Episodes of high carbon dioxide in the blood called hypercapnia
- Respiratory problems including episodes where the child will stop breathing (apnea), difficulty breathing (dyspnea), breathing that is faster than normal (hyperventilation), or different breathing patterns (Chene-Stokes)
- Trouble swallowing called dysphagia
- Eye problems including quick eye movements (nystagmus), crossed eyes (strabismus), problems moving the eye (ophthalmoplegia), breakdown of the nerves of the eyes (optic atrophy), and sight impairment which can lead to blindness
- Structural heart differences such as hypertrophic cardiomyopathy or asymmetric septal hypertrophy

Diagnosis

Leigh syndrome can be diagnosed by:

- Measuring biochemical markers in blood and cerebrospinal fluid - the fluid surrounding the brain and spinal cord
- Brain studies and imaging (brain MRI, CT scan or tomography)
- Careful neurological examination
- Eye examination
- Performing a genetic test

Leigh syndrome is not included on newborn screening panels. If there is a known family history of Leigh syndrome, or parents are known carriers, prenatal testing can be performed on amniotic fluid (the fluid surrounding a baby) or chorionic villi (a specific part of the placenta). Results interpretation of this testing for mitochondrial conditions is complicated and genetic counseling is recommended.

Treatment and Management

Before beginning any treatment or therapy, please consult with your physician.

As of 2022, there is currently no FDA-approved therapy for Leigh syndrome. Treatment and management of Leigh syndrome is symptomatic and supportive and may include:

- Traditional treatment of heart conditions
- Traditional treatment of seizures
- Medications for movement disorders
- Nutrition support
- Physical and occupational therapy
- Avoidance of mitochondrial toxins like certain drugs, tobacco and alcohol
- Mitochondrial supplements like thiamine (vitamin B1)

Individuals living with Leigh syndrome typically work with several healthcare providers regularly, including:

- Neurology for the muscles and brain
- Ophthalmology for the eyes
- Cardiology for the heart
- Physical and occupational therapy
- Registered dietitian

It is important that all those living with or caring for someone with Leigh syndrome have an emergency protocol letter. These letters, which are written and signed by a doctor, share details about prescribed treatment during a crisis and in emergency room settings.

Clinical Trials

For specific details on clinical trials visit www.mitoaction.org/clinicaltrials or www.clinicaltrials.gov.

Resources

- Leigh syndrome - About the Disease – The National Institutes of Health
- Leigh Syndrome - National Organization for Rare Disorders)
- About Leigh Syndrome - People Against Leigh Syndrome

Connecting with others who are impacted by a rare disease allows for important information to be shared about day-to-day life, prevents isolation, and gives hope. Please contact MitoAction for peer support opportunities at 888-MITO-411 or email mito411@mitoaction.org.

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