Leigh Disease

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Introduction

Leigh disease is an inherited early-onset progressive neurodegenerative/ neurometabolic disorder with a characteristic neuropathology consisting of focal, bilateral lesions in one or more areas of the central nervous system, including the brainstem, thalamus, basal ganglia, cerebellum, and spinal cord. The lesions are areas of demyelination, gliosis, necrosis, spongiosis, or capillary proliferation.

Etiology

Leigh's disease can be caused by mutations in mitochondrial DNA or by deficiencies of an enzyme called pyruvate dehydrogenase It may be a feature of a deficiency of any of the mitochondrial respiratory chain complexes: I, II, III deficiencies, complex IV deficiency (cytochrome c oxidase), or complex V deficiency. The most common underlying cause is a defect in oxidative phosphorylation.

Clinical presentations

Clinical symptoms depend on which areas of the central nervous system are involved. This progressive disorder begins in infants between the ages of three months and two years. Rarely, it occurs in teenagers and adults.. Symptoms of Leigh's disease usually progress rapidly. The earliest signs may be poor sucking ability, and the loss of head control and motor skills. These symptoms may be accompanied by loss of appetite, vomiting, irritability, continuous crying, and seizures. As the disorder progresses, symptoms may also include generalized weakness, lack of muscle tone, and episodes of lactic acidosis, which can lead to impairment of respiratory and kidney function. In Leigh's disease, genetic mutations in mitochondrial DNA interfere with the energy sources that run cells in an area of the brain that plays a role in motor movements. The primary function of mitochondria is to convert the energy in glucose and fatty acids into a substance called adenosine triphosphate (ATP). The energy in ATP drives virtually all of a cell's metabolic functions. Genetic mutations in mitochondrial DNA, therefore, result in a chronic lack of energy in these cells, which in turn affects the central nervous system and causes progressive degeneration of motor functions.

Management

The most common treatment for Leigh's disease is thiamine (Vitamin B1). Oral sodium bicarbonate or sodium citrate may also be prescribed to manage lactic acidosis. Researchers are currently testing dichloroacetate to establish its effectiveness in treating lactic acidosis. In individuals who have the X-linked form of Leigh's disease, a high-fat, low-carbohydrate diet may be recommended.

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There is also a form of Leigh's disease (called X-linked Leigh's disease) which is the result of mutations in a gene that produces another group of substances that are important for cell metabolism. This gene is only found on the X chromosome.

Prognosis

The prognosis for individuals with Leigh's disease is poor. Individuals who lack mitochondrial complex IV activity and those with pyruvate dehydrogenase deficiency tend to have the worst prognosis and die within a few years. Those with partial deficiencies have a better prognosis, and may live to be 6 or 7 years of age. Some have survived to their mid-teenage years.

Keywords: Leigh disease; Mitochondropathy; Neurometabolic; Neurodegenerative