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RESEARCH ARTICLE

KRABBE DISEASE

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ABSTRACT

Krabbe disease, also known as globoid cell leukodystrophy or galactosylceramide lipidosis, is an autosomal-recessive sphingolipidosis caused by deficient activity of the lysosomal hydrolase galactosylceramide beta-galactosidase (GALC). GALC degrades galactosylceramide, a major component of myelin, and other terminal beta-galactose–containing sphingolipids, including psychosine (galactosylsphingosine). Increased psychosine levels are believed to lead to widespread destruction of oligodendroglia in the CNS and to subsequent demyelination. There is no cure for Krabbe disease. However, the following treatments may be given to patients to help alleviate their symptoms: anticonvulsant medication to stop seizures, muscle relaxer drugs (to help ease muscle spasms), physical therapy to help slow deterioration of muscles, occupational therapy to help older children with common tasks, such as getting dressed and eating.

INTRODUCTION

Krabbe disease (also called globoid cell leukodystrophy) is a degenerative disorder that affects the nervous system. It is caused by the shortage (deficiency) of an enzyme called galactosylceramidase. This enzyme deficiency impairs the growth and maintenance of myelin, the protective covering around certain nerve cells that ensures the rapid transmission of nerve impulses. Krabbe disease is part of a group of disorders known as leukodystrophies, which result from the loss of myelin (demyelination). This disorder is also characterized by the abnormal presence of globoid cells, which are globe-shaped cells that usually have more than one nucleus.

Meaning

Krabbe originally described a condition with infantile onset that was characterized by spasticity and a rapidly progressive neurologic degeneration leading to death.[3]

Frequency

In the United States, Krabbe disease affects about 1 in 100,000 individuals. A higher incidence (6 cases per 1,000 people) has been reported in a few isolated communities in Israel. Krabbe disease is seen mostly in infants (onset by age 6 months), but it can also develop later in life. Unfortunately, there is currently no cure for Krabbe disease, and most infants with this disease will die before age 2.

Genetic Changes

Mutations in the GALC gene cause Krabbe disease. These mutations cause a deficiency of the enzyme galactosylceramidase. This deficiency leads to a progressive loss of myelin that covers many nerves. Without myelin, nerves in the brain and other parts of the body cannot function properly, leading to the signs and symptoms of Krabbe disease

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- Diffuse Globoid Body Sclerosis
- Galactosylceramidase Deficiency Disease
- Galactosylceramide lipidosis
- GALC deficiency
- GCL
- GLD

Types

Krabbe disease has the following 4 clinical subtypes, distinguished by age of onset: [4]

Type 1 Krabbe disease - Infantile
Type 2 Krabbe disease - Late infantile
Type 3 Krabbe disease - Juvenile

Type 4 Krabbe disease - Adult
Types 2-4 are also referred to collectively as the late-onset subtypes.

Symptoms

Hallmarks of the classic infantile form include irritability, hypertonia, hyperesthesia, and psychomotor arrest, followed by rapid deterioration, elevated protein levels in cerebrospinal fluid (CSF), neuroradiologic evidence of white matter disease, optic atrophy, and early death.

Diagnosis

Genetic Testing

- Genetic Testing Registry: Galactosylceramide beta-galactosidase deficiency
- imaging scans (MRI) of the brain to look for abnormalities
- nerve conduction studies to measure the speed at which electrical impulses are sent through the nervous system
- eye examination to look for signs of damage to the optic nerve

Treatment

For infants who have already developed symptoms of Krabbe disease, there is currently no treatment that can change the course of the disease. Treatment, therefore, focuses on managing symptoms and providing supportive care. Interventions may include the following:

- Anticonvulsant medications to manage seizures
- Drugs to ease muscle spasticity and irritability
- Physical therapy to minimize deterioration of muscle tone
- Nutritional support, such as the use of a tube to deliver fluids and nutrients directly into the stomach (gastric tube)
- Interventions for older children or adults with less severe forms of the disease may include:
- Physical therapy to minimize deterioration of muscle tone
- Occupational therapy to achieve as much independence as possible with daily activities
- Stem cell transplantation

Hematopoietic stem cells are specialized cells that can develop into all of the different types of blood cells in the body. These stem cells are also the source of microglia, specialized debris-eating cells that take up residence in the nervous system. In Krabbe disease, microglia are transformed into toxic globoid cells.

Complications

A number of complications-including infections and respiratory difficulties-can develop in children with advanced Krabbe disease. In the later stages of the disease, children become incapacitated, are confined to their beds and eventually lapse into a vegetative state[3].

Long Term Outlook

The outlook is very poor. On average, infants who develop Krabbe disease will die before age 2. Children who develop the disease later in life will live a bit longer, but typically die between 2 and 7 years after they are diagnosed.

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