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KRABBE DISEASE: A DEGENERATIVE NEUROLOGICAL DISORDER

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ABSTRACT

Krabbe disease is a rare autosomal recessive, inherited genetic disease and usually deadly disorder of the nervous system. Krabbe disease is caused by mutations in the GAC gene locaton chromosome 14 (14q31) . People with Krabbe disease are not able to create enough of a substance called galactosylceramidase, which is needed to make myelin. Myelin is a material the body uses to surround and protect nerve fibers. Without this protection, cells in the brain will die, and the nerves in the brain and other parts of the body will not work properly. Symptoms begin between the ages of 3 and 6 months with irritability, fevers, limb stiffness, seizures, feeding difficulties, vomiting and slowing of mental and motor development. There is no cure for Krabbe disease. However, symptomatic treatments may be given to patients to help alleviate their symptoms. Newer technique as bone marrow transplantation and cord blood stem cells are effective if introduced before onset of symptoms. If there is a family history of Krabbe disease, prenatal tests can be done to screen the fetus for the condition. Genetic counseling is recommended for people with a family history of Krabbe disease if they are considering having children.

Key words: Symptomatic, Krabbe disease, Lysosomal, Leukodystrophy.

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INTRODUCTION

Krabbe disease is originally described as a condition with infantile onset that was characterized by spasticity and a rapidly progressive neurological degeneration leading to death. Since the original description, numerous cases have been documented that show a wide distribution in age of onset [1-3].

Definition

Krabbe disease (KD) (also known as globoid cell leukodystrophy or galactosylceramide lipidosis) is a rare and often fatal lysosomal storage disease which results in progressive damage to the nervous system.

Incidence

Krabbe disease occurs in about one in 100,000 births. A higher incidence, about six in 1,000 has been reported in certain communities in Israel. Scandinavian countries have comparatively high rates of the disease, reported to be one in 50,000 births [4].

Types

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.

Studies indicate that early unrelated hematopoietic stem cell transplantation in both the infantile and late-onset forms is associated with at least short-term benefits on neurocognitive parameters, lifespan, and quality of life. Because of this evidence of success, the addition of Krabbe disease to newborn screening panels has occurred in some states and is under consideration in others [5].

Causes

Krabbe disease is caused when a person inherits two copies of an altered (mutated) gene, one copy from

each parent. Krabbe disease is caused by mutations in the GAC gene locaton chromosome 14 (14q31), which is inherited in an autosomal recessive manner [6].

- Mutations in the GALC gene cause a deficiency of an enzyme called galactosylceramidase.
- In rare cases it may be caused by a lack of active saposin A. The buildup of unmetabolized lipids adversely affects the growth of the nerve's protective myelin sheath (the covering that insulates many nerves) resulting in demyelination and severe progressive degeneration of motor skills. As part of a group of disorders known as leukodystrophies,
- Krabbe disease results from the imperfect growth and development of myelin. GALC deficiency also results in a build-up of a glycosphingolipid called psychosine, which is toxic to oligodendrocytes.

Pathophysiology

Signs and symptoms

In general, the younger the age of onset of Krabbe disease, the faster the disease will progress. People who develop Krabbe disease later in life may have less severe symptoms than infants who get the disease. Infants with Krabbe disease are normal at birth. Symptoms begin between the ages of 3 and 6 months with irritability, fever, limb stiffness, seizures, feeding difficulties, vomiting, and slowing of mental and motor development. In the first stages of the disease, doctors often mistake the symptoms for those of cerebral palsy. Juvenile- and adult-onset cases of Krabbe disease also occur, which have similar symptoms but slower progression [7].

Diagnosis

The disease may be diagnosed by its characteristic grouping of certain cells (multinucleated globoid cells), nerve demyelination and degeneration, and destruction of brain cells. Special stains for myelin (e.g.; luxol fast blue) may be used to aid diagnosis [8].

- A thorough physical examination.
- The sample of blood or skin tissue biopsy, and If GALC activity levels are very low, the child may have Krabbe disease.
- The following tests may also be performed to confirm a diagnosis:
- 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
- Genetic testing to detect the genetic defect that causes Krabbe disease.

Treatment

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 [9].

Newer techniques

Bone Marrow Transplantation

The best results have been only in patients with late-onset Krabbe disease who have been treated before severe symptoms develop. It has not been helpful in infants with early-onset Krabbe disease who have already developed symptoms.

Cord Blood Transfusion

However, this procedure has also been shown to help only those patients treated before symptoms appear.

Nursing management

Possible Nursing diagnosis

- Hyperthermia r/t neurodegenerative disorder
- Pain r/t severe muscle spasm
- Fluid and electrolyte imbalance r/t persistent vomiting
- Imbalanced nutrition r/t feeding difficulties and continuous crying
- Activity intolerance r/t immobility
- Impaired sensory perception r/t deafness and blindness
- Risk of injury r/t seizures

Nursing care

- Assessment of vital sign and neurological functions.
- Assessment of sensory functions for vision and hearing.
- Provide cool environment and tapid sponging for lowering the body temperature
- Encourage more fluids and administer IV fluids to prevent dehydration
- If child is on breast feeding, exclusive breast feeding should be given.
- Encourage frequent feeding, with special care to prevent chocking.
- Feeding should be given in small amount at a time, as child having swallowing difficulty.
- Lie down the baby on hard, flate surface during seizure activity.

- Turn the head to one side for prevention of secretion aspiration.
- Provide a safe and hazard free environment for the child.
- Provide physiotherapy for muscle spasms.
- Proper family support should be given to relieve the stress of parents
- Medications should be given at the proper time daily.
- Occupational therapy should be given according to the child's need and condition.
- Genetic counseling should be given.

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.

Prognosis

In infantile Krabbe disease, death usually occurs in early childhood. A 2011 study found 1, 2, 3 year survival rates of 60%, 26%, and 14%, respectively. A few survived for longer and one was still alive at age 13. Patients with late-onset Krabbe disease tend to have a slower progression of the disease and live significantly longer. Most children who develop Krabbe disease in infancy die before the age of 2, most often from respiratory failure or complications of immobility and markedly decreased muscle tone. Children who develop the disease later in childhood may have a somewhat longer life expectancy, usually between two and seven years after diagnosis

Prevention

- If both parents carry the genetic defect that causes Krabbe disease, there is a 25 percent chance of passing the disease to their child. The 25 percent risk of passing on the disease cannot be lowered if parents both carry the genetic mutation.
- The only way to avoid the risk is if the carriers decide to not have children. The parents can, however, find out if they carry the gene for Krabbe disease through a blood test. If there is a family history of Krabbe disease, prenatal tests can be done to screen the fetus for the condition.
- Genetic counseling is recommended for people with a family history of Krabbe disease if they are considering having children.

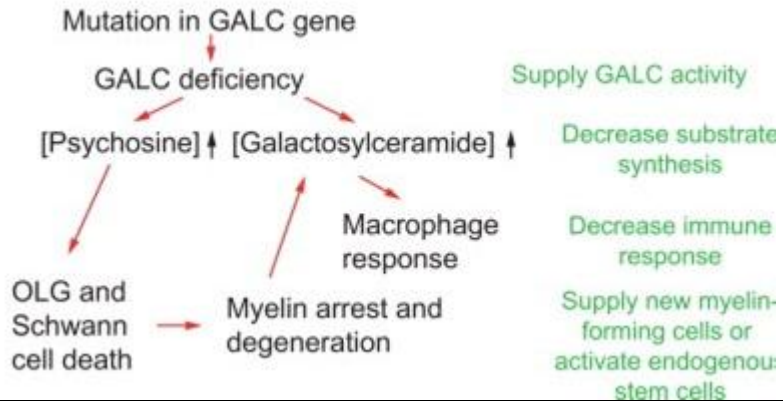
Table 1. Clinical subtypes, distinguished by age of onset

Classification	Early onset	Late onset
Types	Type 1 Krabbe disease - Infantile	• Type 2 Krabbe disease - Late infantile • Type 3 Krabbe disease - Juvenile • Type 4 Krabbe disease – Adult

Table 2. Signs and symptoms of krabbe disease

Classification	a) Early-Onset Krabbe Disease	b) Late-Onset Krabbe Disease	c) Other symptoms
Sign and symptoms	• feeding problems • fevers • persistent vomiting • loss of head control • irritability and excessive crying • poor coordination of movement or stiffness • seizures • muscle spasms (especially arms and legs) • changes in muscle tone • deterioration of mental and motor function • deafness and blindness	• progressive loss of vision leading to blindness • difficulty walking (ataxia) • poor hand coordination skills • muscle weakness or rigid muscle	• Muscle weakness, • spasticity, • deafness, • optic atrophy, • optic nerve enlargement, • blindness, • paralysis, and difficulty when swallowing. • Prolonged weight loss .

Fig 1. Pathogenesis of Krabbe disease and potential sites for corrections.



STATEMENT OF HUMAN AND ANIMAL RIGHTS

All procedures performed in human participants were in accordance with theethical standards of the institutional research committee and with the 1964Helsinki declaration and its later amendments or comparable ethicalstandards. This article does not contain any studies with animals performed by any of the authors.

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Nil

CONFLICT OF INTEREST

None.

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