Krabbe disease

Krabbe disease (also called globoid cell leukodystrophy) is a severe neurological condition. It is part of a group of disorders known as leukodystrophies, which result from the loss of myelin (demyelination) in the nervous system. Myelin is the protective covering around nerve cells that ensures the rapid transmission of nerve signals. Krabbe disease is also characterized by abnormal cells in the brain called globoid cells, which are large cells that usually have more than one nucleus.

The most common form of Krabbe disease, called the infantile form, usually begins before the age of 1. Initial signs and symptoms typically include irritability, muscle weakness, feeding difficulties, episodes of fever without any sign of infection, stiff posture, and delayed mental and physical development. As the disease progresses, muscles continue to weaken, affecting the infant's ability to move, chew, swallow, and breathe. Affected infants also experience vision loss and seizures. Because of the severity of the condition, individuals with the infantile form of Krabbe disease rarely survive beyond the age of 2.

Less commonly, Krabbe disease begins in childhood, adolescence, or adulthood (late-onset forms). Vision problems and walking difficulties are the most common initial symptoms in these forms of the disorder, however, signs and symptoms vary considerably among affected individuals. Individuals with late-onset Krabbe disease may survive many years after the condition begins.

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.

Genetic Changes

Mutations in the *GALC* gene cause Krabbe disease. This gene provides instructions for making an enzyme called galactosylceramidase, which breaks down certain fats called galactolipids. One galactolipid broken down by galactosylceramidase, called galactosylceramide, is an important component of myelin. Breakdown of galactosylceramide is part of the normal turnover of myelin that occurs throughout life. Another galactolipid, called psychosine, which is formed during the production of myelin, is toxic if not broken down by galactosylceramidase.

GALC gene mutations severely reduce the activity of the galactosylceramidase enzyme. As a result, galactosylceramide and psychosine cannot be broken down. Excess galactosylceramide accumulates in certain cells, forming globoid cells. The

accumulation of these galactolipids causes damage to myelin-forming cells, which impairs the formation of myelin and leads to demyelination in the nervous system. Without myelin, nerves in the brain and other parts of the body cannot transmit signals 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
- galactosylcerebrosidase deficiency
- galactosylsphingosine lipidosis
- GALC deficiency
- GCL
- GLD
- psychosine lipidosis

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Galactosylceramide beta-galactosidase deficiency https://www.ncbi.nlm.nih.gov/gtr/conditions/C0023521/

Other Diagnosis and Management Resources

- Baby's First Test http://www.babysfirsttest.org/newborn-screening/conditions/krabbe
- GeneReview: Krabbe Disease https://www.ncbi.nlm.nih.gov/books/NBK1238
- MedlinePlus Encyclopedia: Krabbe disease https://medlineplus.gov/ency/article/001198.htm
- United Leukodystrophy Foundation: Krabbe disease http://ulf.org/krabbe-disease/

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Krabbe disease
  https://medlineplus.gov/ency/article/001198.htm
- Health Topic: Leukodystrophies
  https://medlineplus.gov/leukodystrophies.html
- Health Topic: Newborn Screening
  https://medlineplus.gov/newbornscreening.html

Genetic and Rare Diseases Information Center

- Krabbe disease
  https://rarediseases.info.nih.gov/diseases/6844/krabbe-disease

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Krabbe Disease
  https://www.ninds.nih.gov/Disorders/All-Disorders/Krabbe-Disease-Information-Page
- National Institute of Neurological Disorders and Stroke: Leukodystrophy
  https://www.ninds.nih.gov/Disorders/All-Disorders/Leukodystrophy-Information-Page
- National Institute of Neurological Disorders and Stroke: Lipid Storage Diseases
  https://www.ninds.nih.gov/Disorders/All-Disorders/Lipid-storage-diseases-Information-Page

Educational Resources

- MalaCards: krabbe disease
  http://www.malacards.org/card/krabbe_disease
- Orphanet: Krabbe disease
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=487
- Tulane University
  http://www2.tulane.edu/tnprc/diseases/krabbe/

Patient Support and Advocacy Resources

- Children Living with Inherited Metabolic Diseases
  http://www.climb.org.uk
- Hunter's Hope Foundation
  https://huntershope.org/
- National Organization for Rare Disorders
  https://rarediseases.org/rare-diseases/leukodystrophy-krabbes/
- United Leukodystrophy Foundation
  http://ulf.org

GeneReviews

- Krabbe Disease
  https://www.ncbi.nlm.nih.gov/books/NBK1238

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22krabbe+disease%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Leukodystrophy,+Globoid+Cell%5BMAJR%5D%29+AND+%28Krabbe+disease%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- KRABBE DISEASE
  http://omim.org/entry/245200

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  https://www.ninds.nih.gov/Disorders/All-Disorders/Krabbe-Disease-Information-Page
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  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20301416

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