MAYO CLINIC LABORATORIES

Newborn Screening Act Sheet

Krabbe Disease: Decreased Galactocerebrosidase

Condition Description: Krabbe disease is a lysosomal storage disorder (LSD) and demyelinating disease caused by a deficiency of lysosomal galactocerebrosidase due to mutations in galactocerebrosidase (*GALC*). *GALC* is involved in the normal turnover of myelin and its deficiency leads to dysfunction and eventual loss of oligodendrocytes and Schwann cells. There is wide variability in severity and age of onset. Krabbe disease is an autosomal recessive disorder.

Medical Emergency-Take the following actions:

- Contact family to inform them of the newborn screening result and ascertain clinical status (extreme irritability, stiffness, feeding difficulties, fever with no signs of infection, decreased alertness).
- Consult with genetic metabolic specialist or pediatric neurologist.
- Evaluate the newborn for signs of neurologic dysfunction (see above). If any sign is present or infant is ill, transport to hospital for further evaluation and treatment in consultation with specialist.
- Initiate timely confirmatory/diagnostic testing and management, as recommended by specialist.
- Provide family with basic information about Krabbe disease.

Diagnostic Evaluation: Confirmatory galactocerebrosidase enzyme assay and measurement of psychosine (galactosylsphingosine). Elevations of psychosine support a diagnosis of Krabbe disease. When patients have reduced or absent galactocerebrosidase activity, but psychosine is normal, *GALC* full gene analysis and 30-kB deletion testing should be performed.

Clinical Expectations: The clinical presentation of Krabbe disease ranges from a rapidly progressive early infantile form (EIKD), which is uniformly lethal if untreated, to a more slowly progressive late-onset variant. All disease variants are associated with leukodystrophy but the age of onset and rate of progression vary widely. Molecular genetic analysis of the *GALC* gene may provide information on expected age of first symptoms. Psychosine has been shown to be elevated in patients with clinical signs and symptoms of disease and therefore, may be a useful biomarker for the presence of disease or disease progression. The estimated incidence of EIKD is approximately 1 in 500,000 live births based on newborn screening data. The milder variants are likely more frequent. The only available therapy is hematopoietic stem cell transplantation that is best performed prior to the onset of clinical symptoms. EIKD must therefore be considered a critical, time sensitive newborn screening condition.

Additional Information

Genetics Home Reference

Genetic Testing Registry

Hunter's Hope

Baby's First Test

Mayo Clinic Laboratories Testing

GALCW / Galactocerebrosidase, Leukocytes

PSY / Psychosine, Blood Spot

KRABZ / Krabbe Disease, Full Gene Analysis and Large (30 kb) Deletion, PCR, Varies