Late Onset Krabbe Disease*

(Decreased galactocerebrosidase, *mildly* elevated psychosine)

Condition Description: Krabbe disease (globoid cell leukodystrophy) is a lysosomal disorder caused by deficiency of galactocerebrosidase (GALC) enzyme. It causes impaired turnover of myelin with subsequent dysfunction and eventual loss of oligodendrocytes and Schwann cells.

**There is wide variability in severity and age of onset*.

Differential Diagnosis: Saposin A deficiency.

You Should Take the Following Actions:

- Inform the family of the newborn screening result.
- Ascertain clinical status (newborns are asymptomatic).
- Consult with a pediatric metabolic specialist.
- Evaluate the newborn (perform physical examination, newborns are expected to be asymptomatic).
- Initiate further diagnostic testing, as recommended by the specialist.
- Provide the family with basic information about **Late Onset Krabbe disease** and its management.

Diagnostic Evaluation: Leukocyte galactocerebrosidase (GALC) enzyme assay and measurement of erythrocyte psychosine (PSY) concentration: Decreased enzyme activity is suggestive of Krabbe disease. However, this result alone does ***not*** exclude pseudo deficiency, which causes decreased enzyme levels without disease.

Combined evaluation of galactocerebrosidase activity ***and*** psychosine concentration predict the phenotype (unaffected vs. early-onset vs. late-onset Krabbe disease). Molecular genetic testing can help confirm the diagnosis.

Clinical Considerations: This screening result is more likely associated with the **Late Onset** forms of Krabbe disease. But all forms of Krabbe disease are associated with leukodystrophy with age of onset and rate of progression varying widely.

Treatment: The only available therapy is hematopoietic stem cell transplantation that is best performed prior to the onset of clinical symptoms. Gene therapy and other clinical trials may be available.

Online resource: Krabbe Disease | Newborn Screening

Krabbe carriers and Pseudo-deficiency alleles

(False-positive newborn screening results)

Secondary and confirmatory lab results indicated your patient is a carrier of Krabbe Disease or has a GALC pseudo-deficiency allele.

What does it mean to be a carrier of Krabbe disease?

Carriers of Krabbe disease are individuals who have a variant (mutation) in one of their two *GALC* genes. These individuals still have one *GALC* gene without a mutation.

Carriers of Krabbe disease should not have any signs or symptoms of Krabbe disease.

However, there is a 1 in 4 (25%) chance a carrier may have a child with Krabbe disease if their partner is also a carrier of Krabbe. Both parents of a child with Krabbe disease are nearly always carriers of the condition.

What does it mean to have a pseudo-deficiency allele?

False-positive newborn screening results for this condition may happen. Some babies with decreased GALC enzyme levels have a “pseudo-deficiency allele”. Pseudo-deficiency means the baby’s GALC enzyme levels were low on the screening but are normal in their body. These babies do **not** have Krabbe disease.

Patients with only a pseudo-deficiency allele do not have (and should never develop) Krabbe disease.

In very rare cases, babies may have positive newborn screening result for Krabbe disease, and have a different disease called Saposin A deficiency.

Where can I find more information?

Internet References: http://www.babysfirsttest.org/