Suggested Follow-up for Decreased GALC enzyme with Elevated Psychosine

Condition Description:

Krabbe disease (also known as globoid cell leukodystrophy) is a very rare neurological disorder. It is caused by a deficiency of Galactocerebrosidase (GALC enzyme) which leads to an accumulation of Psychosine (a highly cytotoxic lipid). The disease results in 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. The infantile form usually presents before the first months of life. Newborns are asymptomatic and, if left untreated, survival beyond 2 years of age is uncommon.

Note: *Krabbe disease is an autosomal recessive disorder. Krabbe carriers and patients with pseudo-deficiency alleles (false positives) may also be identified in the initial screening test*.*

You should take the following IMMEDIATE actions:

- Inform the family of the combined GALC ***and*** Psychosine (PSY) lab results.
- Evaluate the newborn (perform physical examination; newborns are expected to be asymptomatic).
- If PSY is > 1 **nmol/L**, consult with and refer to a pediatric metabolic specialist promptly.
- **If PSY is ≥ 10 nmol/L, consult with and refer to a pediatric transplant specialist the SAME DAY and refer to a metabolic specialist.**
- Initiate additional confirmatory/diagnostic testing, as recommended by the specialists.
- Provide the family with basic information about Krabbe disease.
- The attached handout "*When Baby has a decreased GALC and an elevated Psychosine"* may be used for this purpose.
- Report final diagnostic outcomes to the SC DHEC Newborn Screening program.

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

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

Clinical Considerations: The clinical presentation of Krabbe disease ranges from a rapidly progressive infantile form to more slowly progressive later-onset variants. All forms of Krabbe disease are associated with leukodystrophy. However, the age of onset and rate of progression vary widely.

Treatment: The only available therapy is hematopoietic stem cell transplantation (**HSCT**). It is most effective if performed ***before 30 days of life*** in patients with the infantile form, or prior to the onset of clinical symptoms in the late-onset forms. Gene therapy and other clinical trials may be available.

Differential Diagnosis: Saposin A deficiency, which has been described in <10 patients, is clinically very similar to Krabbe disease and may also be detected by newborn screening.

Internet Resources: **https://www.acmg.net/PDFLibrary/Krabbe-Infantile.pdf**

https://www.acmg.net/PDFLibrary/Krabbe-Later-Onset.pdf

*Referral Resources/ List of providers at GGC, MUSC, and Duke**

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NOTE: This list is not inclusive of all prospective providers