Newborn Screening ACT Sheet

Absent/Reduced Biotinidase Activity

Biotinidase Deficiency

Differential Diagnosis: Biotinidase deficiency; see C5-OH for non-biotinidase associated conditions.

Metabolic Description: Biotinidase deficiency results from defective activity of the biotinidase enzyme. When identified (possibly) through elevated C5-OH, 3-hydroxyisovaleric acid and 3-methylcrotonylglycine are elevated, and holocarboxylase synthase deficiency must be considered.

You Should Take the Following Immediate Actions

- Contact family to inform them of the newborn screening result and ascertain clinical status (poor feeding, lethargy, hypotonia).
- See and evaluate infant.
- Consultation/referral to a metabolic specialist to determine appropriate follow-up. (See attached list.)
- If infant cannot be seen immediately by a metabolic specialist, undertake confirmatory testing in consultation with a metabolic specialist.

- Initial testing: Enzyme Assay for Biotinidase.
- Repeat newborn screen if second screen has not been done.
- Begin Biotin treatment if symptomatic.
- Report findings to newborn screening program.

Confirmation of Diagnosis: Enzyme assay for biotinidase reveals low activity. Plasma acylcarnitine analysis may show normal or increased 3-hydroxyisovaleric acid and 3-methylcrotonylglycine. C5-OH acylcarnitine may be high, but lack of an abnormal acylcarnitine profile does not rule out biotinidase deficiency.

Clinical Expectations: The neonate is usually asymptomatic, but episodic hypoglycemia, lethargy, hypotonia, and mild developmental delay can occur at any time from the neonatal period through childhood. Untreated biotinidase deficiency leads to developmental delay, seizures, alopecia, and hearing deficits. Biotinidase may normalize on the second screen on affected babies, therefore an infant with an out of range first newborn screen and normal second newborn screen will still need an enzyme assay. Biotin treatment is available and highly effective.

Reporting: Report diagnostic result to family and NBS program.

Additional Information:

National Center for Biotechnology Information

OMIM
http://omim.org/entry/253260

Genetics Home Reference

Disclaimer: This information is adapted from American College of Medical Genetics website ACT sheets 05/2015