ACMG
American College of Medical Genetics and Genomics
Translating Genes Into Health®

ACT Sheet

Newborn Screening ACT Sheet

[Elevated C5-OH Acylcarnitine]

Organic Acidemias

Differential Diagnosis: 3-methylcrotonyl-CoA carboxylase (MCC) deficiency, maternal MCC deficiency, 3-hydroxy-3-methylglutaryl-CoA lyase (HMG) deficiency; ß-ketothiolase (BKT) deficiency; multiple carboxylase deficiency (MCD) (holocarboxylase synthetase deficiency [HCS] or biotinidase deficiency [BTD]), 2-methyl-3-hydroxybutyric acidemia (MHBD), 3-methylglutaconic aciduria (MGA), and MT-ATP6 related mitochondrial disorders.

Condition Description: Elevated C5-OH is associated with a group of organic acid disorders caused by a deficiency of an enzyme involved in the catabolism of branched chain amino acids. In most of the disorders, potentially toxic metabolites accumulate with variable clinical presentations. Each of the disorders is caused by a deficiency of the relevant enzyme. Of these disorders, MCC deficiency is the most common. HMG and HCS deficiencies can present acutely in the neonatal period.

You Should Take the Following IMMEDIATE Actions:

- Inform family of the newborn screening result.
- Ascertain clinical status (poor feeding, vomiting, lethargy).
- Consult with pediatric metabolic specialist the same day.
- Evaluate the newborn (hypoglycemia, ketonuria, metabolic acidosis). If any of these findings are present or if the newborn is ill, transport to a hospital for further treatment in consultation with the metabolic specialist.
- Initiate confirmatory/diagnostic testing as recommended by the specialist.
- Provide the family with basic information about the possible diagnoses and their management, including the need for urgent treatment of metabolic acidosis.

- Report final diagnostic outcome to newborn screening program.

Diagnostic Evaluation: Plasma acylcarnitine profile: C5-OH is elevated in all conditions; C5:1 (tiglylcarnitine) is also elevated in BKT deficiency. Urine organic acids demonstrate abnormal patterns characteristic of each condition. Urine organic acids and plasma acylcarnitines performed on infant and mother *are* warranted to evaluate for maternal MCC deficiency. Serum biotinidase: identifies biotinidase deficiency. Plasma amino acids: may demonstrate reduced citrulline in MT-ATP6-related disorders. Enzymatic and molecular genetic testing may be required.

Clinical Considerations: MCC deficiency is the most common of these disorders and most individuals with this diagnosis remain asymptomatic. Neonates with HMG and HCS deficiencies can present acutely with feeding difficulties, hypotonia, lethargy, and seizures; avoidance of fasting in these neonates is essential. Clinical features vary among the other conditions and can include episodes of hypoglycemia, lethargy, and hypotonia occurring during infancy and/or childhood. MGA comprises a heterogenous group of disorders associated with diminished mitochondrial function. MT-ATP6-related mitochondrial disorders have been associated with Leigh syndrome, a neurodegenerative disorder. There is treatment available that is specific to each condition.

Additional Information:

How to Communicate Newborn Screening Results
Emergency Protocols (New England Consortium of Metabolic Programs) (HMG | MCC)
Gene Reviews (BTD)
Medline Plus (HMG | MCC | BKT | HCS | BTD | MGA | MT-ATP6-related mitochondrial disease/Leigh syndrome)
Condition Information for Families- HRSA Newborn Screening Clearinghouse (HMG | MCC | BKT | MCD | HCS | BTD | MGA)

Referral (local, state, regional, and national):

Find a Genetics Clinic Directory
Genetic Testing Registry

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