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

ACT Sheet

Newborn Screening ACT Sheet

[Elevated C5-DC Acylcarnitine]

Glutaric Acidemia Type I (GA I)

Differential Diagnosis: None.

Condition Description: Glutaric acidemia Type I (GA I) is caused by deficiency of glutaryl-CoA dehydrogenase, an enzyme in the lysine degradation pathway, leading to elevated glutaric acid, glutarylcarnitine (C5-DC) and other toxic metabolites. Neonatal presentation is rare, but affected patients are at high risk of neurodegenerative crises triggered by common childhood illnesses.

You Should Take the Following IMMEDIATE Actions:

- Inform family of the newborn screening result
- Ascertain clinical status (poor feeding, macrocephaly, hypotonia).
- Consult with pediatric metabolic specialist.
- Evaluate the newborn (poor feeding, macrocephaly, hypotonia).
- Initiate confirmatory/diagnostic testing and management, as recommended by the specialist.
- Provide family with basic information about GA-I and its management.

- Report findings to newborn screening program.

Diagnostic Evaluation: Urine organic acids: Glutaric and 3-hydroxyglutaric acids are typically elevated in GA I but may be only mildly elevated or have normal levels in some affected individuals. Plasma acylcarnitines will demonstrate elevated glutarylcarnitine (C5-DC). Urine glutarylcarnitine (C5-DC): may help identify patients with GA I who have low glutaric acid excretion by urine organic acid analysis. Molecular genetic testing can confirm the diagnosis.

Clinical Considerations: Neonates with GA I typically do not have acute symptoms but can be macrocephalic, most often presenting later in infancy. This disorder typically manifests as an acute encephalopathic crisis triggered by an intercurrent infectious illness, fasting, or other stressors. Rarely children may present with a chronic cerebral palsy presentation without an apparent acute metabolic crisis. Presymptomatic initiation of treatment can prevent the onset of irreversible neurologic symptoms. Treatment includes a diet low in lysine, carnitine supplementation, and emergency treatment during intercurrent illness with the goal of averting catabolism. Untreated late onset GA I (> 6 years of age) may manifest with other nonspecific neurologic abnormalities including headaches, vertigo, dementia and ataxia. Even with treatment all patients with GA I may be at increased risk for additional manifestations (e.g. renal disease). An infant with GA I presenting with macrocephaly and a subdural hematoma may phenotypically mimic shaken baby syndrome.

Additional Information:

How to Communicate Newborn Screening Results
Gene Reviews
Medline Plus
Condition Information for Families- HRSA Newborn Screening Clearinghouse

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

Find a Genetics Clinic Directory
Genetic Testing Registry

State and Other Resources

State Newborn Screening Program

Newborn Screening Program, Utah Department of Health and Human Services
801-584-8256, newbornscreening.health.utah.gov/

Genetics/Metabolic Consultants

Pediatric Medical Genetics, University of Utah Department of Pediatrics
801-213-3599, healthcare.utah.edu/pediatrics/programs-services/genetics.php

Information for Clinicians and Families

Utah Medical Home Portal (see Newborn Disorders and Parents & Families sections)
ut.medicalhomeportal.org/newborn/glutaric-acidemia-type-1

Parent/Family Support

Organic Acidemia Association
www.oaanews.org/ga-i.html

National Resources (with web addresses)

Additional Information

How to Communicate Newborn Screening Results
www.hrsa.gov/sites/default/files/hrsa/advisory-committees/heritable-disorders/Resources/achdnc-communication-guide-newborn.pdf

Gene Reviews
www.ncbi.nlm.nih.gov/books/NBK546575/

Medline Plus
medlineplus.gov/genetics/condition/glutaric-acidemia-type-i/

Condition Information for Families-HRSA Newborn Screening Clearinghouse
newbornscreening.hrsa.gov/conditions/glutaric-acidemia-type-i

Genetic and Rare Diseases Information Center
rarediseases.info.nih.gov/diseases/10321/3-methylglutaconyl-coa-hydratase-deficiency-auh-defect

Referral (local, state, regional and national)

Find a Genetics Clinic Directory
clinics.acmg.net

Genetic Testing Registry
www.ncbi.nlm.nih.gov/gtr/