

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 <u>IMMEDIATE</u> 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: <u>Urine organic acids</u>: 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. <u>Plasma acylcarnitines</u> will demonstrate elevated glutarylcarnitine (C5-DC). <u>Urine glutarylcarnitine (C5-DC)</u>: may help identify patients with GA I who have low glutaric acid excretion by urine organic acid analysis. <u>Molecular genetic testing</u> 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

This practice resource is designed primarily as an educational resource for medical geneticists and other clinicians to help them provide quality medical services. Adherence to this practice resource is completely voluntary and does not necessarily assure a successful medical outcome. This practice resource should not be considered inclusive of all proper procedures and tests or exclusive of other procedures and tests that are reasonably directed to obtaining the same results. In determining the propriety of any specific procedure or test, the clinician should apply his or her own professional judgment to the specific clinical circumstances presented by the individual patient or specimen. Clinicians are encouraged to document the reasons for the use of a particular procedure or test, whether or not it is in conformance with this practice resource. Clinicians also are advised to take notice of the date this practice resource was adopted, and to consider other medical and scientific information that becomes available after that date. It also would be prudent to consider whether intellectual property interests may restrict the performance of certain tests and other procedures.

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State and Other Resources

State Newborn Screening Program

Nevada Newborn Screening Program, Nevada State Public Health Laboratory 775-682-6238, med.unr.edu/nsphl/newborn-screening

Genetics/Metabolic Consultants

Nicola Longo, MD, PhD, University of Utah Genetics/Pediatrics 801-585-2457, healthcare.utah.edu/fad/mddetail.php?physicianID=u0305101

Information for Clinicians and Families

Nevada Medical Home Portal (see Newborn Disorders and Parents & Families sections) nv.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/achdnccommunication-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/

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