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

ACT Sheet

Newborn Screening ACT Sheet

[Elevated C16-OH +/- C18-OH]

Long-chain 3-Hydroxyacyl-CoA Dehydrogenase (LCHAD) Deficiency

Differential Diagnosis: Mitchondrial Trifunctional Protein (TFP) deficiency.

Condition Description: LCHAD and TFP deficiencies are fatty acid oxidation (FAO) disorders that disrupt fatty acid breakdown at the level of long-chain fatty acids. They are associated with characteristic elevations in long-chain acylcarnitines predominantly C16-OH acylcarnitine, and with decreased energy production from fats, particularly during periods of prolonged fasting or increased energy demands (fever, stress) when energy production relies increasingly on fat metabolism. Neonates can present with severe cardiomyopathy.

You Should Take the Following IMMEDIATE Actions:

- Inform the family of the newborn screening result.
- Ascertain clinical status (poor feeding, lethargy, vomiting, hypotonia) and elicit a history of acute fatty liver and/or preeclampsia in the mother and of sudden unexpected death in a sibling.
- Consult with pediatric metabolic specialist the same day.
- Evaluate the newborn (lethargy, hepatomegaly, hypoglycemia, arrythmias, cardiac insufficiency). 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. If the newborn becomes even mildly ill (poor feeding, vomiting, lethargy), immediate treatment with IV glucose is indicated. Initiate confirmatory/diagnostic testing and management as recommended by specialist.
- Provide the family with basic information about LCHAD/TFP deficiencies and its management, including the need for the infant to avoid fasting.
- Report final diagnostic outcome to newborn screening program.

Diagnostic Evaluation: Plasma acylcarnitines: C16-OH and C18-OH (and to a lesser extent, other long chain acylcarnitines) are characteristically elevated in LCHAD and TFP deficiencies. Molecular genetic testing is required to differentiate between these two disorders and confirm the diagnosis. If clinically indicated, consider an immediate echocardiogram.

Clinical Considerations: LCHAD and TFP deficiencies may present acutely in the neonate and are associated with high mortality rates unless treated promptly. Features include hepatomegaly, cardiomyopathy, arrythmias, lethargy, hypoketotic hypoglycemia, elevated liver transaminases, elevated creatine phosphokinase (CPK), lactic acidosis and rhabdomyolysis. Later onset forms with milder phenotypes can occur. Treatment should be initiated under the guidance of a specialist and includes the avoidance of fasting and supplementation with medium-chain triglycerides.

Additional Information:

How to Communicate Newborn Screening Results
Emergency Protocols (New England Consortium of Metabolic Programs)
GARD (LCHAD | TFP)
Medline Plus (LCHAD | TFP)
Condition Information for Families- HRSA Newborn Screening Clearinghouse (LCHAD | TFP)
ClinGen Actionability Report

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

Find a Genetics Clinic Directory
Genetic Testing Registry

Local Resources *(Insert Local Website Links)*

State Resource Site (Insert Website Information)

Name	
URL	
Comments	

Local Resource Site (Insert Website Information)

Name	
URL	
Comments	

Appendix *(Resources with Full URL Addresses)*

Additional Information

How to Communicate Newborn Screening Results

- https://www.hrsa.gov/sites/default/files/hrsa/advisory-committees/heritable-disorders/resources/achdnc-communication-guide-newborn.pdf

Emergency Protocols (New England Consortium of Metabolic Programs)

- https://www.newenglandconsortium.org/lchadd

GARD

- https://rarediseases.info.nih.gov/diseases/6867/lchad-deficiency
- https://rarediseases.info.nih.gov/diseases/3684/mitochondrial-trifunctional-protein-deficiency

Medline Plus

- https://medlineplus.gov/genetics/condition/long-chain-3-hydroxyacyl-coa-dehydrogenase-deficiency/
- https://medlineplus.gov/genetics/condition/mitochondrial-trifunctional-protein-deficiency/

Condition Information for Families-HRSA Newborn Screening Clearinghouse

- https://newbornscreening.hrsa.gov/conditions/long-chain-3-hydroxyacyl-coa-dehydrogenase-deficiency
- https://newbornscreening.hrsa.gov/conditions/mitochondrial-trifunctional-protein-deficiency

ClinGen Actionability Report

- https://actionability.clinicalgenome.org/ac/Pediatric/ui/stg2SummaryRpt?doc=AC1039

Referral (local, state, regional and national)

Find a Genetics Clinic Directory

- https://clinics.acmg.net

Genetic Testing Registry

- https://www.ncbi.nlm.nih.gov/gtr/

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