TEXAS Department of State Health Services

Newborn Screening ACT Sheet

Elevated C4 Acylcarnitine

Short-Chain Acyl-CoA Dehydrogenase Deficiency (SCAD) / Isobutyrylglycinuria (IBG)

Differential Diagnosis: Short-chain acyl CoA dehydrogenase (SCAD) deficiency; Isobutyrl-CoA dehydrogenase (IBDH) deficiency; Ethylmalonic encephalopathy (EE); isobutyrylglycinuria (IBG).

Condition Description: SCAD deficiency is a fatty acid oxidation (FAO) disorder. FAO occurs during prolonged fasting and/or periods of increased energy demands (fever, stress) when energy production relies increasingly on fat metabolism. IBG results from IBDH deficiency. IBDH is an enzyme involved in the degradation of the branched chain amino acid valine. EE is a related disorder that seems to be due to a defective mitochondrial matrix protein, the precise function of which is yet unknown. In all three conditions, potentially toxic metabolites accumulate.

You should take the Following Actions:

- **Contact family to inform them of the newborn screening result and ascertain clinical status (poor feeding, vomiting, lethargy).**
- **Consult with pediatric metabolic specialist. (See attached list.)**
- **Evaluate the newborn (hypoglycemia, lethargy, metabolic acidosis).**
- **Emergency treatment if symptomatic**
- **Initiate timely confirmatory/diagnostic testing as recommended by specialist.**
- **Initial testing: plasma acylcarnitine profile, urine organic acids, urine acylglycines.**
- **Repeat newborn screen if the second screen has not been done.**
- **Educate family about need for infant to avoid fasting, and explain signs, symptoms and need for urgent treatment if infant becomes ill.**
- **Report findings to newborn screening program.**

Diagnostic Evaluation: In SCAD deficiency urine organic acids show increased ethylmalonic acid. In IBG, plasma and urine acylcarnitines will show increased isobutyrylcarnitine (C4-acylcarnitine) and urine organic acids/acylglycine may show isobutyrylglycine. In Ethylmalonic Aciduria (EMA), plasma acylcarnitine analysis will typically show increased C4- and C5-acylcarnitine and urine organic acids/acylglycine analysis will show increased EMA and isovalerylglycine. Molecular genetic analysis to confirm the suspected diagnosis is possible for these conditions.

Clinical Considerations: SCAD deficiency can have a variable presentation. Most affected neonates are asymptomatic. An affected neonate however, can be extremely ill with vomiting, lethargy, seizures, and hypoketotic hypoglycemia. Treatment consists primarily of avoidance of fasting and vitamin/cofactor supplementation. Isobutyrl-CoA dehydrogenase deficiency may be benign (anemia and cardiomyopathy has been reported in one case). EMA encephalopathy presents in infancy with developmental delay, diarrhea and petechiae.

Additional Information:

American College of Medical Genetics and Genomics
https://www.acmg.net/StaticContent/ACT/C4.pdf

Genetics Home Reference
http://ghr.nlm.nih.gov/condition/short-chain-acyl-coa-dehydrogenase-deficiency

STAR G FELSI
http://www.newbornscreening.info/Pro/fattyaciddisorders/SCADD.html
http://www.newbornscreening.info/Parents/fattyaciddisorders/SCADD.html