Glutaric Acidemia Type 1

The above named patient has Glutaric Acidemia Type 1 (GA1). GA1 is an inborn error of metabolism in which the amino acids lysine, hydroxylysine and tryptophan are not broken down properly. Without treatment, patients with GA1 are at increased risk of developing neurological typically before 6 years of age. The risk for an acute encephalopathic crisis is frequently precipitated by gastroenteritis, intercurrent febrile illness, immunization, or surgical intervention. Metabolic management includes a low lysine diet, carnitine supplementation and intensified emergency treatment during acute episodes of intercurrent illness.

Affected patients with GA1 are at greatest risk for metabolic decompensation when one or more of the following are present:

1) Intercurrent illness in particular when food/fluid intake is less than 75% of normal
2) Recurrent vomiting and/or diarrhea
3) Prolonged fasting
4) Weight loss of more than 10%
5) High fever
6) Trauma and/or surgery

The following symptoms may be a sign of metabolic decompensation:

Drowsiness, lethargy, refusal to feed, vomiting, seizures, changes in behavior, hypotonia, irritability, rigor, dystonia
MINOR ACUTE ILLNESS (temperature is <101 degree Fahrenheit, upper airway infection, child tolerating oral intake, no alteration in consciousness)

1) Start sick-day formula provided by the metabolic center; this formula contains increased calories and does not contain lysine (should not be given solely for >48 hours)

2) Increase the dose of oral L-carnitine to 200 mg/kg/day

3) Re-assess situation every 2 hours regarding state of consciousness, fever, and feed tolerance; if situation worsens, have patient evaluated in pediatric ER

4) Antipyretics may be given if temperature is >101 degree Fahrenheit

If the patient has recurrent vomiting, recurrent diarrhea, reduced intake of nutrients, spiking temperature or concerning neurological signs, emergency treatment is required at a hospital.

ACUTE ILLNESS EMERGENCY PROTOCOL AT HOSPITAL

1) A patient with GA1 must be evaluated immediately

2) Assess the patient clinically
   If the patient is unconscious or lethargic immediately start infusion with 10% glucose followed by blood sampling.

3) Glucose infusion rates:
<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Glucose (g/kg per day IV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1</td>
<td>(12-15)</td>
</tr>
<tr>
<td>1-3</td>
<td>(10-12)</td>
</tr>
<tr>
<td>3-6</td>
<td>(8-10)</td>
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<tr>
<td>6-10</td>
<td>(6-8)</td>
</tr>
<tr>
<td>&gt;10</td>
<td>3-6</td>
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</tbody>
</table>

If persistent hyperglycemia>150 mg/dL (> 8 mmol/L) and/or glucosuria occurs, start with 0.05 IE insulin/kg per h IV and adjust the infusion rate according to serum glucose.

4) Draw bloods for CBC, blood gas, e’lytes, calcium, phosphate, liver enzymes, free and total carnitine, creatinine, urea nitrogen, C-reactive protein, amino acids (in the recovery phase), blood culture (if applicable), amylase/lipase (in severe disease for pancreatitis), creatine kinase (in severe disease for rhabdomyolysis). Check urine for ketone bodies and pH.

5) If tolerated orally, increase L-carnitine dose to 200 mg/kg/day. Otherwise start I.V. L-carnitine 100 mg/kg/day.
6) Stop natural intake of proteins for 24 (-48) hours and then reintroduce and increase stepwise until the amount of maintenance treatment is reached in 48 (-72) hours. If tolerated start sick day formula that does not contain lysine and contains reduced amount of tryptophan as early as possible.

7) Treat any underlying illness or symptom (infection, dehydration, vomiting) as indicated. Use antipyretics in case of fever.

8) If acidosis alkalination of urine with sodium bicarbonate facilitates urinary excretion of organic acids

9) Monitor heart rate, blood pressure, temperature, diuresis; Glasgow Coma Scale if reduced consciousness; assessment for neurological signs (hypotonia, irritability, rigor, dystonia)

10) Immediately notify the on-call UM Geneticist at 305-331-3023. This is a 24/7 service

Disclaimer: the above recommendations cannot replace an individual medical evaluation by a board certified physician. The UM Geneticist on-call should always be informed. UM is not responsible in case the protocol has not been followed.

Above protocol was modified from Kölker et al., J Inherit Metab Dis. 2011;34:677-94.