Metabolic Genetics Service, Division of Medical Genetics, University of Utah

Guidelines for diagnosis, evaluation, management

Note: use as shared baseline (set of defaults), modify as needed for individual patients

Updated 14 Aug 2019/ NL/AA/LB

MSUD – Maple Syrup Urine Disease

Lab Diagnosis:

1. Plasma amino acids (send to ARUP): alloisoleucine, with increased branched chain amino acids (leu>ile>val). Can be normal in intermittent form.
    a. Alloisoleucine can be seen in IVA but high leucine is not seen in this condition.
2. Urine Organic acids; 2-oxoacids of branched chain AA. Can have high ketones in acute event (can also be seen by UA). Look for additional abnormalities (also in urine) in E3 defects.
3. DNA to confirm diagnosis and define specific subtype
4. Skin biopsy if DNA testing is inconclusive or if VUS

Inpatient Management:

1. Work up at diagnosis: URGENT visit, see as soon as possible because of neonatal presentations with brain edema
    a. Physical examination: check fontanel, tone, alertness, check ear wax for maple syrup odor.
    b. Labs: Plasma amino acids, BMP (for sodium, anion gap), urine ketones, urine organic acids
    c. Imaging: consider head CT (or MRI) if concerned for increased intracranial pressure
2. Treatment
    a. Leucine decreases about 400-500uM per day with proper treatment
    b. If child is conscious and tolerating enteral feeds: Start NG tube to provide MSUD formula only x 48 hours
        i. Then add isoleucine and valine supplements after 48 hours
        ii. Start at 100mg each, can go up to 200mg each pending amino acids
            - Reduce back to 100mg when adding back in intact protein
        iii. Calorie goals: 110-120kcal/kg
        iv. At 4-5 days restart natural protein at 0.7g/kg
        v. Zofran with vomiting
    c. If child is unconscious start IV fluids and intralipids
        i. Start D10 normal saline + 20mEq KCl at maintenance rate + 4g/kg/day 20% intralipids (20ml/kg/day)
            - Sodium goal on CMP: >140 mEq/L
            - Consider giving bolus
            - Calorie goals: 110-120kcal/kg
        ii. Obtain central line and start: D20 normal saline + 20 mEq KCl at maintenance rate +4g/kg/day 20% intralipids (20ml/kg/day)

iii. Start insulin if necessary 0.1unit/kg bolus, followed by the same dose as a drip/hour to keep glucose 70-150mg/dL.
iv. If unable to tolerate enteral feeds when needing to start back natural protein: start TPN with 0.5g/kg trophamine.

d. If signs of brain edema and/or sodium drops below 135 mEq/L: give 0.5g/kg Mannitol followed by 3% NaCl (1ml/kg)
    i. Repeat hypertonic NaCl as necessary

3. Monitoring
    a. Daily CMP and PAA

Outpatient Monitoring

1. Emergency protocol to parents, pediatrician, electronic medical record
    a. Consider medical alert bracelet
2. Branch-chain restricted diet : May need supplemental VAL, ILE
    a. leucine to normal range (60 to 230 uM; <300 for best outcomes)
        i. Washout for Leucine above 800uM
    b. normal to slightly high isoleucine (normal 30-130; acceptable <200)
    c. normal to slightly high valine (normal 140-350)
    d. VAL to LEU ratio close to 1:1.
3. Thiamine: trial thiamine (start 100mg BID) for three months. if thiamine trial is negative, still consider thiamine (50mg/d, as 25mg BID) if anemic
4. Carnitine: supplements not routine, monitor levels as needed (because of protein restriction) and supplement if below normal range.
5. Visit schedule:
    a. Initial visit
    b. 2 weeks
    c. Monthly x 3 months
    d. Q3 months up to 1.5-2 years of age
    e. Q6months up to 18 years
    f. Yearly after 18 years
6. Visit assessments: clinical (including skin), growth, development (milestones, Denver)
    a. formal neuropsychologic evaluation at 2 and 6 years (as in PKU/GAL)
7. Visit labs: QPAA, BMP at every visit.
    a. Add once a year or more frequently as needed (because of protein-restricted diet) vitamin D 25OH, CBC with diff, iron status (ferritin, serum iron, iron saturation), calcium, phosphorus, prealbumin.
    b. Consider DEXA scan (age, fractures)
8. Monitoring between visits: keep well hydrated
    a. Monitoring labs:
        i. 0-12 months: every 1-2 weeks
        ii. 1-3 years: 1-2 months
        iii. >3 years: every 1-3 months
        iv. As necessary for metabolic control, diet changes and illness.
9. Sick Day Diet

a. Obtain CMP, PAA, UA
    i. Consider UA or urine ketone strips at home for monitoring (trace or small okay)
b. If vomiting, prescribe Zofran
c. Restrict natural protein by 50-100% x 24-48 hours
d. Continue medical food, increase calories to 120% (medical food, prophree, gatorade, sugar, etc).
e. Continue valine and isoleucine supplements – do not increase beyond home range (100-200mg/day).
f. If not able to tolerate feeds or liquids, seek ER care.

Monitoring endpoints:

1. Growth: Length/height, weight, OFC centiles and velocity should be normal
2. Development: normal motor and language, check for impairments/disabilities
    a. Neurocognitive testing: 3 years, 6 years, 8 years, 12 years and 18 years
3. Physical exam: normal (isoleucine deficits can cause dermatitis-like manifestations)
4. Reduce hospitalizations, decompensations, ED visits
5. Laboratory: leucine, Ileu, valine normal (leucine <plasma amino acids)
6. Nutritional labs: vitamin D 25 OH, vitamin B12, ferritin, zinc as needed
7. Imaging (brain MRI): only if clinically indicated