Altered mental status is a very common presentation to the ED among all age groups. The differential is extremely broad, ranging from pedestrian infections and intoxications to exotic diseases. In this case, we have a rare presentation of metabolic disease, which is often not considered outside of the pediatric population.

**Case Description**

A 19 year-old woman was brought into the ED for bizarre behavior and hypersomnolence after a weekend out with friends. Grandparent noted no prior history of behavioral issues or impairments, but mentioned family history of mental illness. Over the course of one week, patient demonstrated bizarre behavior—appropriately responses, poor concentration, and disheveled appearance—leading up to her becoming excessively sleepy and lethargic.

On exam she had normal vital signs; she was sleepy but arousable to verbal stimuli; no scleral icterus, hepatosplenomegaly or meningeal signs were identified; and she had no focal neurologic deficits. She was oriented to name, place, and time, but was unable to concentrate for simple calculation, recall items, or perform visuospatial reasoning.

Urine toxicology and serum alcohol were negative. Blood counts, liver panel, urine analysis, cerebral spinal fluid, chest x-ray, and head computer tomography were all normal. Chemistry panel showed normal electrolytes and creatinine, but revealed a low blood urea nitrogen (2 mg/dL). Ammonia level was elevated at 250 μmol/L. The patient’s primary hyperammonemia was treated with lactulose while the remainder of the workup was completed. Within 48 hours, the ammonia level down trended concomitantly with her recovery to normal appearance. Once lucid, she reported a recent pregnancy that had resulted in a miscarriage.

Toxicology consultants checked a VPA level to exclude surreptitious valproic acid intoxication. Genetics found a negative Ornithine Transcarbamylase (OTC) screen.

After lactulose was discontinued, patient relapsed and was admitted with an ammonia level over 250 μmol/L. Outpatient testing of plasma quantitative amino acid was suggestive OTC deficiency.

**Discussion**

**Pathophysiology**

- Ammonia is generated from the breakdown of nitrogenous substances in the gut and from the use of glutamine as a metabolic fuel in the small intestine.
- The liver detoxifies ammonia by converting it to urea and to a lesser extent, glutamine.
- Hyperammonemia develops when portal blood from the intestines bypasses the liver (secondary) or when the urea cycle within hepatocytes functions poorly (primary). In the setting of normal liver function, a defect in the urea cycle must be suspected.
- Late-onset defects typically manifest after a stress event—grave infection/illness, dehydration, gross dietary change, or pregnancy have been reported.

**Diagnosis Workup**

- **Common symptoms:** rapid development of lethargy, hypothermia, hyperventilation, cerebral edema, seizures, and/or coma.
- **Lab Studies:** Liver Panel, Chemistry Panel, VPA, Urinary Organic Acids Plasma Quantitative Amino Acids, Urinary Orotic Acid. (See Algorithm).

**Flowchart**

- ** AMS**
  - Plasma Ammonia >150 μMol/L
  - Elevated Arginine (ASL Deficiency)
  - Elevated Arginosuccinate (ASL Deficiency)
- **Normal Anion Gap, Normal Liver Panel, Normal Glucose, and Low BUN**
  - Low Citrulline/Arginine
  - Absent Arginosuccinate (ASS Deficiency)
- **Negative VPA**
  - Elevated Citrulline
  - Elevated Urinary Orotic Acid (OTC Deficiency)
  - Low Urinary Orotic Acid (CPSI or NAGS Deficiency)