Hyperammonemia in a child with short bowel syndrome: urea cycle disorder or complication of altered gastrointestinal function?

Rachel VanCoillie, DO; Laura Konczal, MD

Hyperammonemia is an acute condition frequently encountered in the field of biochemical genetics and can result from a variety of underlying etiologies. While many of these etiologies are inborn errors of metabolism, hyperammonemia can result from various acquired causes. Elevated ammonia levels have also been recognized in adult patients who have undergone bariatric surgery or have short bowel syndrome, thought to be related to a combination of catabolism from decreased intake, malabsorption and decreased synthesis of nutrients (including urea cycle intermediates and essential amino acids required for anabolism), and altered intestinal microbiota. However, to our knowledge, this phenomenon has not before been demonstrated in the pediatric population.

Here we present a 4-year old male with a history of short bowel syndrome secondary to malrotation with volvulus as an infant, episodes of D-lactic acidosis, and esophageal strictures who presented to the hospital with headaches, emesis, and progressive lethargy and was found to have an elevated ammonia level of 397 umol/L. Subsequent biochemical laboratory work-up was significant for an elevated urine orotic acid of 133.5 mmol/mol Cr and globally low plasma amino acids but disproportionately decreased plasma arginine (7 umol/L) and plasma citrulline (5 umol/L) concerning for a urea cycle disorder, particularly for Ornithine Transcarbamylase (OTC) Deficiency. However, molecular testing via a hyperammonemia panel was negative.

Initial management included rifaximin, lactulose, 10% dextrose at 1.5 times maintenance rate, intralipids 1g/kg/day, and an IV ammonia scavenger. He was later transitioned to an enteral ammonia scavenger and supplementation with enteral citrulline. His original enteral protein goals were 1.5g/kg/day to balance the need for low protein with a potential urea cycle disorder and malabsorption from short bowel syndrome. However, plasma amino acid levels remained low until TPN was initiated and the amino acid concentration in the TPN alone was increased to 1g/kg/day. After these interventions, his ammonia has not been elevated and his nutritional status has greatly improved on normal amounts of protein, TPN, citrulline, and the enteral ammonia scavenger. Since the patient has done so well on TPN receiving the RDI of protein for age and his genetic testing was negative, it brings into question whether the hyperammonemia and orotic aciduria was related to altered gastrointestinal function as opposed to an inborn error of metabolism.