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Case report

Hyperammonemic encephalopathy complicating bariatric surgery: A case study and review of the literature

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Bariatric surgery for obesity has become more common, with 220,000 cases performed in the United States each year [1]. Hyperammonemic encephalopathy is a rare but potentially devastating condition. A total of 7 cases of hyperammonemic encephalopathy after bariatric surgery have been reported in the literature to date; in 5 of these, the outcome was fatal. A number of mechanisms may underlie the cause of hyperammonemia. Importantly, early active treatment may be life-saving.

Case report

A 52-year-old female with a background history of anxiety underwent a series of bariatric surgical procedures for obesity. Gastric banding was initially performed in 1999 but failed to produce adequate weight loss. To address this, a subsequent biliopancreatic diversion with a 75-cm common channel was performed in 2003. However, this was complicated by poor oral intake, malnutrition, and psychiatric disturbances, including an admission to hospital with the diagnosis of catatonic schizophrenia. Her weight had dropped from 128 kg to 60 kg. She underwent revision of the biliopancreatic diversion (with lengthening of the common channel from 75 cm to 225 cm to increase her absorptive capacity) in 2005.

In 2009 after regaining weight to 128 kg, she underwent laparoscopic surgery to reduce the volume of her remaining stomach and excise some redundant small bowel at the gastroenterostomy. She was well in the immediate postoperative period, comfortably able to eat a small plate of food at each meal, and was discharged home. However, she presented 5 months later with fatigue and cognitive changes requiring admission. During this admission, she became overtly encephalopathic with a precipitously decreased level of consciousness requiring intubation and ventilation in an intensive care unit. Her ammonia level was found to be elevated at 155 μmol/L (<30 μmol/L), despite transaminases that were either normal or borderline elevated (ALT 25 g/L, AST 43 g/L). Albumin was 18 g/L, and total protein was 43 g/L. Coagulation parameters were normal. She was treated with supportive care and lactulose. Her condition improved, and she was discharged from hospital but subsequently fluctuated with 4 further episodes of hyperammonemic encephalopathy requiring 2 separate prolonged admissions.

At the subsequent admission, she was treated with oral metronidazole, cholestyramine, and erythromycin for possible blind loop syndrome. *Klebsiella pneumonia* was isolated on a single occasion from urine culture but multiple blood cultures were negative. An abdominal Doppler ultrasound was negative for portal hypertension. Although the patient had a body mass index of 32 kg/m^2, she had signs of nutritional deficiency with pitting edema, fine hair, and dry skin. Investigations revealed plasma amino acids to be uniformly decreased or near the

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lower limit of normal excepting glutamine, which was in the middle of the reference range, while plasma carnitines were normal (Table 1). After a further episode of hyperammonemic encephalopathy, she was managed with a combination of sodium benzoate and arginine, high intravenous calories from lipid and dextrose, but moderate protein intake diet. Notably, hypoglycemia had never been documented at any stage.

Exclusion of genetic abnormalities: Urinary organic and amino acids were unremarkable on multiple occasions, including during episodes of encephalopathy, without abnormalities of orotic acid, citrulline, or arginine to suggest a genetic disorder of the urea cycle. Sequencing of the *CPS1* (carbamyl phosphate synthase 1) and *NAGS* (N-acetyl-glutamate synthase) genes excluded these disorders of the urea cycle that can only be reliably diagnosed on molecular testing.

Although the liver was not thought to be failing from other causes of chronic liver disease, autoimmune, infectious, and Wilson disease were also excluded. At this stage, it was concluded that the hyperammonemic episodes were purely due to malnutrition with consequent inhibition of the urea cycle.

She accordingly underwent a reversal of her weight loss surgery in 2011. Her gastroenterostomy was taken down and the upper and lower gastric remnants were reanastomosed, restoring gastric continuity. The entero-enterostomy from the previously revised bilio-pancreatic diversion was also taken down and small bowel continuity reestablished from duodenum to cecum without any segmental small bowel bypass. Her symptoms resolved, her biochemical parameters thereafter progressively normalized and she has had no further episodes of hyperammonemia.

Table 1
Plasma levels, amino acids, and derivatives

Amino acid or derivative	Value		Normal range
Total carnitine	42	µmol/L	21–70
Acetylcarnitine	10	µmol/L	3–31
Free carnitine	31	µmol/L	13–56
Glycine	247	µmol/L	119–368
Ornithine	36	µmol/L	26–102
Phenylalanine	31	µmol/L	30–75
Alanine	100	µmol/L	131–600
Aspartic acid	4	µmol/L	3–11
Arginine	28	µmol/L	34–118
Asparagine	29	µmol/L	22–81
Citrulline	19	µmol/L	10–45
Cysteine:homocysteine	Interference		0–3
Cystine	6	µmol/L	24–67
Glutamate	48	µmol/L	11–99
Glutamine	448	µmol/L	385–862
Histidine	138	µmol/L	47–113
Homocystine	Not Detected		0.0–.2
Isoleucine	17	µmol/L	34–106
Lysine	82	µmol/L	84–260
Methionine	10	µmol/L	12–43
Serine	58	µmol/L	68–182
Taurine	52	µmol/L	29–104
Threonine	26	µmol/L	53–237
Tyrosine	12	µmol/L	32–114
Valine	72	µmol/L	108–314
Leucine	38	µmol/L	56–178

Boldface indicates level outside normal range.

Discussion

Neurologic complications of bariatric surgery, the most common of which is peripheral neuropathy, are usually attributed to nutritional shortfalls such as vitamin B12 and thiamine deficiency [2,3]. Minor neurologic complications occur reasonably frequently, with an incidence of up to 15% in a retrospectively controlled study [4]. The presentation of hyperammonemic encephalopathy can include psychiatric disturbances (as demonstrated by our patient), confusion, nausea and vomiting, and progressive loss of consciousness secondary to cerebral edema. Hyperammonemic encephalopathy related to bariatric surgery has only been described in 3 publications [5–7], although the authors are anecdotally aware of a number of other cases.

Ammonia is a toxic by-product of protein and energy metabolism that is produced in all body tissues. Its disposal is through the urea cycle (Fig. 1), whereby it is converted to urea for excretion via the kidneys and large intestine. The full urea cycle predominantly occurs in the liver although the kidney also has some activity. Potential causes for hyperammonemia in the setting of bariatric surgery include: digestive or urinary tract infection with urease producing bacteria, medications (particularly sodium valproate), bacterial overgrowth in a blind loop of bowel, porto-systemic shunting, or unmasking of a genetic disorder of the urea cycle [6]. Each of these had been adequately excluded in our patient, leaving functional inhibition of the urea cycle as the most likely cause.

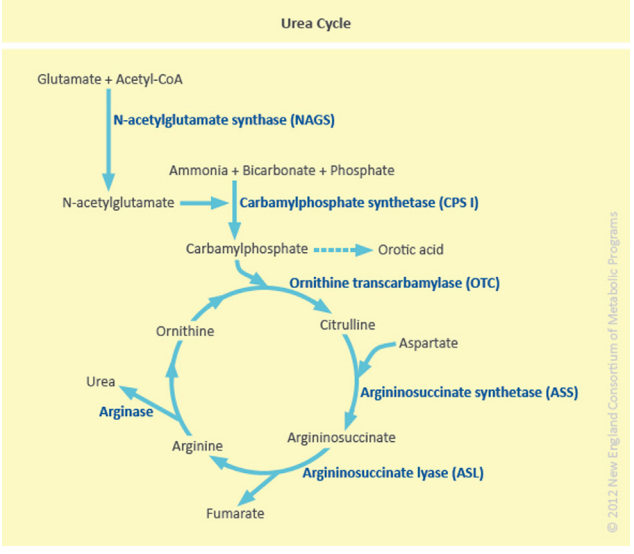

Fig. 1. The urea cycle.