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CASE REPORT | ENDOSCOPY

Postbariatric Surgery Hyperammonemia: A Rare Cause of Encephalopathy

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ABSTRACT

Hyperammonemic encephalopathy is an under-recognized and potentially fatal complication of Roux-en-Y gastric bypass surgery. We present a case of a 42-year-old woman with no known history of liver disease who experienced worsening encephalopathy 1 year after bariatric surgery. She presented with elevated ammonia and severe encephalopathy requiring intubation. A complete workup led to the diagnosis of a urea cycle disorder. The patient was managed with lactulose, ammonia scavenging agents, and nutritional supplementation with a favorable outcome. We report this case to increase awareness of this condition and urge providers to maintain a high clinical suspicion in the appropriate setting.

INTRODUCTION

Hyperammonemic encephalopathy is a relatively common clinical encounter. Less commonly, it will present in the absence of overt liver disease, particularly in the postbariatric surgery patient.[1–4] Referred to as gastric bypass-related hyperammonemia (GaBHA) by Fenves et al, this syndrome poses a potentially fatal and under-recognized complication.[1,2,4,5] Several underlying mechanisms have been proposed including occult genetic aberrations and impaired function of the urea cycle, which become unmasked in the presence of an anatomically altered digestive system, nutritional deficiencies, and a heightened catabolic state.[3–5] Manifestations of GaBHA range from mild confusion to coma and can present at varying postoperative intervals.[3,4] Treatment is aimed at reducing ammonia levels while providing nutritional support to keep up with an increased metabolic demand.[3,5] Mortality has been reported to be as high as 50%.[2,4] Early diagnosis and intervention can improve the outcomes. With the obesity epidemic persisting and gastric bypass surgery as a potential treatment, a high clinical suspicion for GaBHA is crucial.[1–3]

CASE REPORT

A 42-year-old woman with a medical history of anxiety and obesity (body mass index 31 kg/m^2) was transferred to our hepatobiliary transplant facility for encephalopathy resistant to treatment with lactulose. The patient was minimally arousable and had seizures; thus, she was immediately intubated. The family was able to provide her history. Since an elective Roux-en-Y gastric bypass 1 year earlier, the patient complained of dyspepsia, nausea, and vomiting that resulted in poor oral intake. The patient also had personality changes consisting primarily of irritability. She was started on buspirone by her primary care physician for anxiety but discontinued the medication because she felt it was ineffective. She was not on any medications for 3 months before this hospitalization. Two months before this visit, the patient's irritability progressed to confusion and lethargy, intermittent at first and then constant. The week before hospitalization, the patient was sleeping for most of the day and had difficulty remembering simple facts, which prompted them to bring her to the emergency department.

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Initial workup showed hyperammonemia and transaminitis. The patient had no known liver disease and did not consume alcohol. The family provided the records of an outpatient liver biopsy, performed for unclear reasons 2 months back, that showed mild chronic periportal inflammation and moderate macrosteatosis without cirrhosis. Additional outpatient records were not available for review. Her acetaminophen level and urine drug screen were negative. Brain computed tomography was unremarkable. Abdominal/pelvic computed tomography showed fatty liver without cirrhosis. Blood and urine cultures were collected. The patient was started on intravenous thiamine and rectal lactulose and was admitted to the intensive care unit. Further workup excluded Wilson disease, hemochromatosis, and viral and autoimmune hepatitis. Because of the suspicion of a urea cycle disorder, specific studies were obtained, and Hepatology was consulted. The results of these studies and pertinent initial laboratory results are provided in Table 1.

Blood cultures revealed a polymicrobial (*Escherchia coli*, methicillin-sensitive *Staphylococcus aureus*, and *Enterococcus faecalis*) bacteremia. Urine culture grew *Enterococcus* species. On hospital day 3, the patient was started on intravenous vancomycin and piperacillin/tazobactam. On the same day, the patient was started on sodium benzoate/sodium phenylacetate, rifaximin, zinc, and arginine through a nasogastric tube. She also was started on supplemental parenteral lipids and glucose. That evening, she started to follow commands, and the next day, she was successfully extubated. Over the next few days, ammonia and liver enzymes normalized and mentation returned to baseline. The patient was discharged home to complete a course of intravenous antibiotics. She was counseled on a protein-restricted diet and was instructed to follow-up with outpatient hepatology. Genetic counseling was advised and has not yet been completed.

Table 1. Laboratory values

	Value	Reference range
White blood cells, K/μL	6.2	4.2–11.1
Hemoglobin, g/dL	11.4	11.4–15.1
Hematocrit, %	32.8	36.1–45.4
Platelets, K/μL	328	130–400
Blood urea nitrogen, mg/dL	11	7–18
Creatinine, mg/dL	0.65	0.55–1.02
Total bilirubin, mg/dL	1.9	0.2–1
Aspartate aminotransferase, U/L	169	15–37
Alanine transaminase, U/L	182	13–61
Alkaline phosphatase, U/L	132	45–117
Albumin, g/dL	1.7	3.4–5
Total protein, g/dL	5.8	6.4–8.2
Prothrombin time, s	13	9–12.5
International normalized ratio	1.24	<1.1
Ammonia, μmol/L	190	11–32
Cyclic citrullinated peptide, U/mL	<0.5	0.0–2.99
Urine orotic acid	5.78	Reference range not established
Orotic acid/creatinine ratio, mmol/mol	1.63	0.11-1.07
Vitamin B12, pg/mL	>2,000	211–911
Vitamin A, μg/dL	26	20–65
25-hydroxy vitamin D, pg/mL	27.7	19.9–79.3
Free carnitine, μmol/L	14	20–55
Total carnitine, μmol/L	22	27–73
Carnitine esters	0.6	0.00–0.09
Manganese	None detected	Reference range not established

DISCUSSION

Ammonia is a neurotoxic byproduct of protein metabolism. The urea cycle converts this byproduct into urea. In normal functioning metabolic processes, urea is produced mainly in the liver, then released into circulation, and ultimately excreted in the urine and digestive tract.[5,6] When this process becomes impaired, ammonia builds up in the bloodstream and can lead to hyperammonemic encephalopathy.[6]

There are various ways in which the urea cycle can become impaired, including cirrhosis, nutritional deficiencies, or enzymatic dysfunction.[4,6,7] Enzymopathies usually manifest early on, placing a urea cycle disorder low on the list of differentials for a hyperammonemic adult. Our case illustrates a population in which a high suspicion should be maintained. Encephalopathy can range from mild personality changes to coma. Subtle symptoms can be misdiagnosed as psychiatric disturbances.[1,4] Our patient had personality changes that were attributed to anxiety. These changes may have been early signs of encephalopathy.

Liver disease is a well-known cause of hyperammonemic encephalopathy. Although she did not have documented cirrhosis, our patient did have fatty liver. A case report by Grogg et al also had a patient with fatty liver and a similar disease course.[8] It is unclear whether fatty liver predisposes patients to GaBHA or whether this is an incidental finding that is more likely to occur in an obese population. Further studies should investigate whether fatty liver is a risk factor for GaBHA.

Infection can also cause encephalopathy. Our patient had bacteremia but was never septic. She showed dramatic improvement hours after starting aggressive ammonia-reducing therapy, at which point she had received less than 12 hours of antibiotics. We feel infection was not the main cause of encephalopathy but rather contributed to a heightened catabolic state, which exacerbated the problem.

Carnitine deficiency can rarely cause hyperammonemia as well. Patients usually present with hypoglycemia and

improve with carnitine supplementation.[9,10] Despite low carnitine levels, our patient improved without carnitine supplementation.

Last, it was not until a thorough discussion with the patient's family that we were able to illicit that the onset of symptoms began after bypass surgery. We encourage clinicians to use investigative skills and conduct thorough interviews. We advocate for provider–family relationships that may improve patient care. In reporting this case, we also aim to increase awareness of GaBHA. Although Roux-en-Y gastric bypass is no longer the most commonly performed bariatric surgery in the United States, in other countries, it remains a common practice (11). Providers should have a low threshold for checking serum ammonia, and GaBHA should be considered in the right context because this potentially fatal complication can be aggressively managed with favorable outcomes.

DISCLOSURES

Author contributions: All authors contributed equally to writing this manuscript. Y. Goltser is the article guarantor.

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Informed patient consent was obtained for this case report.

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