Acute Psychotic Disorder After Gastric Bypass Surgery: Differential Diagnosis and Treatment

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Many psychiatric complications after gastric bypass surgery, such as severe psychotic disorders, Wernicke's encephalopathy, and Korsakoff's syndrome, have been reported in the medical literature. Gastric bypass surgery, also known as bariatric surgery or gastroplasty for morbid obesity, has gained popularity because of the obesity epidemic in this country (1). Morbid obesity, which correlates with a body mass index (weight [kg]/height [m]^2) of 40 or higher, is a chronic, intractable disease that, if left untreated, results in morbidity, mortality, and a decreased lifespan (2). Traditional nonsurgical weight-loss methods that attempt to decrease weight through dietary and behavioral interventions often result in disappointing outcomes with a high rate of relapse (3). Therefore, the popularity of surgical treatment for weight loss has increased. Surgery to treat morbid obesity was recognized by the National Institutes of Health in 1998 as an approach for well-informed and motivated patients for whom the surgical risks are acceptable (4, 5). Using the 2000 National Health Interview Survey database, Livingston (6) estimated that over 5 million Americans (2.8% of the U.S. population) met eligibility criteria for gastric bypass surgery using the standard definition of morbid obesity. Buckwald et al. (1) estimated that 5% of the U.S. population meets these criteria at present. Overall, the number of gastric bypass surgeries performed annually increased from about 16,000 in the early 1990s to about 103,000 in 2003 (7).

Operations available for the treatment of morbidly obese patients include simple operations that restrict the amount of food a patient can eat as well as more complex operations that bypass portions of the digestive tract to create a degree of malabsorption. The two surgical weight-loss procedures most commonly performed in the United States for morbid obesity are gastric bypass, also known as the Roux-en-Y gastric bypass, and vertical banded gastroplasty (2, 8). The Roux-en-Y gastric bypass is both restrictive (i.e., limits the amount of solid food the patient is able to ingest) and malabsorptive (i.e., decreases intestinal absorption). During a Roux-en-Y gastric bypass, staples are used to construct a small restrictive upper gastric pouch that then is anastomosed directly to the small intestine, usually bypassing 40–60 cm, although some surgeons may bypass greater lengths of small intestine for increased weight reduction. Vertical banded gastroplasty is a restrictive procedure in which staples are used to create a small stomach pouch with no rerouting of the digestive tract. Both procedures can be performed laparoscopically. Vomiting and reflux are common risks associated with both procedures, and nutritional deficiencies and "the dumping syndrome" occur at higher rates in patients who have Roux-en-Y gastric bypass (7).

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Although it is believed to be a safe procedure, life-threatening psychiatric complications associated with rapid weight reduction and hyperemesis can occur after gastric bypass surgery. These complications can be insidious, and clinical presentations vary along a spectrum from neurological abnormalities to psychiatric manifestations. Such variability is thought to be related to the individual vulnerability of the CNS to nutritional decline or possibly the length of time until medical evaluation and treatment. Lack of awareness of complications and their symptoms can result in delays in diagnosis and effective treatment. The following case of a patient who developed acute psychosis 52 days after gastric bypass surgery illustrates some of the complexities encountered in managing such a situation.

Case History

Mr. A was a 39-year-old Caucasian man who became acutely psychotic 52 days after gastric bypass surgery and after a 3-day course of transdermal scopolamine to control nausea during a cruise.

History of Present Illness

Mr. A had experienced frequent episodes of vomiting when he attempted to eat solid food after his gastric bypass surgery and had experienced more rapid weight

loss than recommended, but he had been psychiatrically well until 52 days after his surgery. While aboard a cruise ship, he developed psychotic symptoms, including his description of feeling subjectively "weird," experiencing auditory and visual hallucinations, and demonstrating intermittent odd and aggressive behaviors. He became loud, sleepless, argumentative, and involved in altercations with the ship's captain. He was evacuated from the cruise ship and hospitalized in the Caribbean, where he was treated for 3 days with haloperidol and benzodiazepines. His symptoms were initially attributed to the use of a transdermal scopolamine patch to prevent seasickness, which he had worn for 6 days. It was discontinued without any resolution of his symptoms.

Mr. A was transferred to a psychiatric facility in the United States; unfortunately, because of a policy at the Caribbean hospital, the records accompanying him were limited to a letter from the ship's captain and did not include the specific doses of medications he received while there. During his first U.S. hospitalization, all medications were discontinued, and he was discharged after a day without receiving any psychotropic medications and while he was functioning normally, according to his wife and to his discharge information. After 2 normal days at home, he became agitated and required psychiatric readmission. His 13-day course at the second U.S. hospitalization was characterized by periods of clarity alternating with aggressiveness, confusion, hallucinations, and delusions. Medical causes of delirium, including infection, stroke, tumor, and electrolyte imbalance, were investigated without revealing a cause. Additionally, an EEG was conducted to evaluate the possibility of delirium and temporal lobe epilepsy, but the study results were normal, and, demonstrated no evidence of slowing. Mr. A was treated with liquid valproic acid (500 mg in the morning, and 1000 mg at bedtime) and dissolvable sublingual olanzapine (5 mg b.i.d. and 10 mg at bedtime) and was discharged to an intensive outpatient psychiatric program where he became increasingly agitated and was unable to tolerate the treatment.

He eloped on the second day and was found wandering in the pouring rain, covered in mud, and actively hallucinating. He was taken directly to our emergency department. He had been given diagnoses of "normal," "seizure secondary to scopolamine," and "bipolar disorder secondary to seizure" from these hospitalizations. Detailed cognitive assessments of Mr. A were not documented in those hospital records. In the emergency department, he reported feeling "a little off" at times, hallucinating, and feeling as if he would die. Upon examination, he described hyperreligious thoughts and derealization. He was repeatedly observed to shout hyperreligious phrases. He was often disoriented, demanding, and restless; his affect was flat. He was unable to complete most of the items on the Folstein Mini-Mental State Examination (MMSE), but he spelled "world" backward without error and recalled two of three objects at 5 minutes. A neurological examination in the emergency department revealed mild ataxia and weakness on the left side.

Past Medical and Psychiatric History

Upon further review, Mr. A's wife indicated that he had experienced intermittent disorientation lasting 1 or 2 days while receiving transdermal scopolamine 5 years earlier, which she felt was quite different from his symptoms this time. Three years before the hospitalization, he had been diagnosed with ocular myasthenia gravis, for which he underwent thymectomy and was subsequently symptom-free without the use of any cholinergic agents or medications.

Fifty-two days before the onset of his psychosis, he had undergone laparoscopic Roux-en-Y gastric bypass surgery with a 100-cm small intestinal bypass for obesity. Postoperative care included diet supplementation with multivitamins and vitamin B_{12}, but he vomited frequently. He had lost 46.4 kg (102.1 lb) since the surgery (134.1 kg [295.0 lb] before the gastric bypass surgery and 87.7 kg [192.9 lb] by admission). There was no past substance abuse or psychiatric history (other than the previous scopolamine reaction by Mr. A) in the patient, his mother, or his wife. Mr. A's wife recalled that during the cruise, she had noted him to have abnormal eye movements, such as rotatory nystagmus, and difficulty with memory and word finding.

Social and Family History

Mr. A was a college graduate with a bachelor's degree in hotel/restaurant management. He had held jobs managing a hotel in Manhattan, working at a gym, working with his brother, and now singing karaoke professionally on weekends. He had been married for 5 years and lived with his wife and two children. He had been the primary caregiver for the children at his own wish on weekdays while his wife worked as a representative of a drug company. He sang on stage on weekends and some evenings. His conversion from Judaism to Methodism 5 years ago had not been accepted by his mother and siblings. There was no family history of psychiatric illness.

Hospital Course

During a prolonged hospitalization on a locked psychiatric ward, Mr. A continued to exhibit intermittent confusion, hallucinations, agitation, and aggression. He frequently attempted to elope from the ward and placed himself and the staff in danger of physical harm on a number of occasions. For instance, he ran into a reinforced glass window in a heavy wooden door after pushing four staff members away and sustained multiple cuts on his body and a 10-cm laceration on his scalp requiring urgent care. His cognitive function was severely impaired early in his hospital course, with scores on the MMSE of less than 10 of 30. He also demonstrated frequent staring episodes, a paucity of speech, memory deficits, tachycardia, orthostatic hypotension, and episodes of presyncope. Olanzapine (dissolvable sublingual), up to 30 mg/day; valproic acid (as a liquid formulation), up to 1500 mg/day; and quetiapine, up to 800 mg/day, were among the key psychotropics initially tried, but they did not improve his symptoms. Frequent administration of intramuscular haloperidol and intramuscular lorazepam, as needed, were effective for sedation, but they also did little to ameliorate his symptoms. Loxapine (oral concentrate), up to 100 mg b.i.d., along with 50 mg every 6 hours, as needed, for agitation was eventually used with some success in controlling his agitation. However, his confusion, hallucinations, and cognitive deficits persisted. His orthostatic hypotension and tachycardia were not corrected by intravenous fluid resuscitation.

Mr. A required frequent small meals because of his gastric bypass surgery; however, because of his fluctuating mental status and frequent vomiting, his oral intake became very poor and his weight continued to drop to a nadir of 81.8 kg (180.0 lb). A barium swallow study demonstrated severe gastroesophageal reflux and a small (2×2 cm) gastric pouch but no other abnormalities. He received parenteral supplementation of multivitamins, thiamine, and folic acid, but total parenteral nutrition was not pursued because of concerns about the safety of central-line placement and maintenance given his mental status. During the fifth week of hospitalization, after 1.5 weeks of taking loxapine and after two unsuccessful attempts at placement of a fluoroscopically guided nasojejunal tube for nutrition, an upper endoscopy was performed and demonstrated severe (2 mm) stenosis of the surgical anastomosis, which was not visible even retrospectively on the barium swallow. After dilation of the stenosis, Mr. A's nausea and vomiting resolved, and his oral intake rapidly improved within 1–2 days. His confusion and agitation gradually diminished, and his cognition improved after the resolution of vomiting and assured oral intake. His MMSE scores improved to 28 of 30 7 weeks after admission, but he still had mild short-term memory deficits, trouble recalling the date, and occasional hallucinations. A brief trial (three sessions) of ECT was performed 10 weeks after admission but was not considered effective.

Mr. A was discharged with close follow-up after a 13-week stay. One month after discharge, Mr. A began reducing his psychotropic medications, i.e., loxapine, 100 mg every 12 hours, and lamotrigine, 100 mg every 12 hours; at this time, he did not have hallucinations but still had mild short-term memory difficulties. At 6-month follow-up, he was not taking any psychotropic medications and had returned to his full level of premorbid functioning. His weight has been maintained at 86.4–88.6 kg (190.1–194.9 lb).

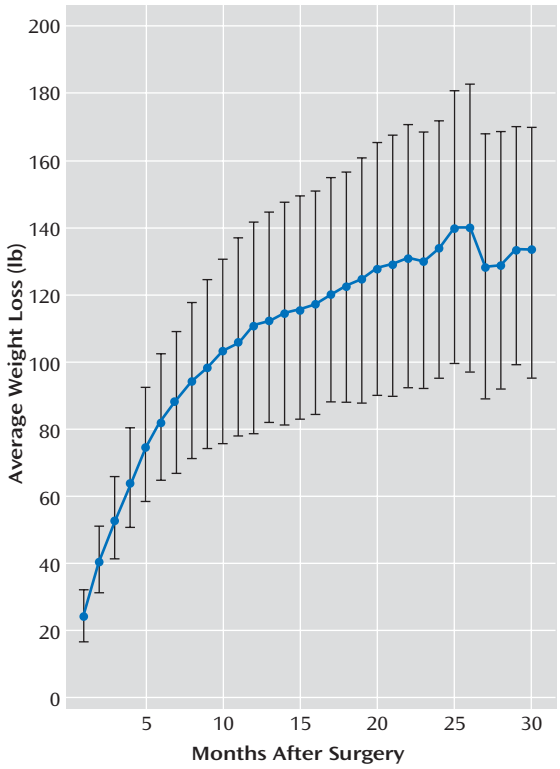
Discussion

Diagnostic Challenges

The patient was hospitalized psychiatrically and cared for by physicians trained in internal medicine and psychiatry. Because of his age, an absence of a past psychiatric history, and a lack of prodromal symptoms, along with his complete recovery without antipsychotic medications, we do not believe this patient had a primary psychotic disorder, such as schizophreniform or delusional disorder. Psychosis and delirium due to a general medical condition were considered. An extensive medical evaluation was undertaken, including routine laboratory studies, a paraneoplastic panel, a toxicology screen, brain and body imaging, an EEG, and a lumbar puncture. His only abnormal laboratory test upon admission was a low albumin level (3.0 g/dl). Unfortunately, laboratory values from the patient's initial visit to the Caribbean facility were not attainable, although verbal communication with the physicians who had seen the patient indicated that his initial values and toxicology screens had been negative. Scopolamine-induced psychosis was initially suspected. Patients with myasthenia gravis are more prone to scopolamine-induced psychosis, but this patient's myasthenia gravis had been limited to ocular symptoms, and after a thymectomy, he had not had any symptoms or required medications. Furthermore, the literature suggests that psychotic symptoms triggered by transdermal scopolamine diminish rapidly after discontinuation, with 11 days being the longest reported duration of psychosis after discontinuation (9, 10). Scopolamine-induced psychosis had been considered at the Caribbean hospital, but physostigmine was not administered, and the duration of the patient's symptoms seemed to be much more prolonged than in any reported cases (11). Despite rapid removal of the transdermal scopolamine, our patient's psychosis continued, which is atypical for scopolamine-induced psychosis, according to the available literature. Additionally, his EEG was normal, which is unusual in cases of delirium or anticholinergic toxicity (see, e.g., http://www.psych.org/psych_pract/treatg/pg/pg_delirium.cfm). In this instance, our patient's symptoms improved substantially only after correction of surgical anastomotic stenosis, cessation of vomiting, supplementation of thiamine, and optimal nutrition. It is possible that use of the scopolamine patch may have triggered the rapid onset or increased the severity of the psychosis related to his rapid weight reduction and hyperemesis after gastric bypass surgery. Without use of the patch, his psychotic symptoms might have begun more insidiously.

Psychotic manifestations after gastric bypass surgery have been reported by many groups (12–15). Others have reported similar psychotic symptoms in patients after gastrectomy (16), a hunger strike (17), and a crash diet for weight loss (18). Such episodes of psychosis are frequently classified as Wernicke's encephalopathy (19–21), pseudochorea (22), or encephalopathy (23). The question of Wernicke's encephalopathy versus another form of psychotic disorder (primary or secondary) was heavily debated by the physicians treating this patient, especially in the absence of consistent neurological manifestations. The classic triad in Wernicke's encephalopathy—i.e., confusion, ophthalmoplegia, and ataxia—is well known; however, simultaneous presence of the full triad is rare. In a series of patients with Wernicke's encephalopathy, the full triad of symptoms was reportedly present in only 0%–29% (24–26). The authors emphasized that Wernicke's encephalopathy most commonly appears as an "organic mental syndrome" with confusion, disorientation, memory impairment, and dyscalculia, with or without peripheral neuropathy, and rarely with eye signs or ataxia (26). Our patient demonstrated apparent apathy, hallucinations, confusion/agitation, and cardiovascular dysfunction. Ataxia was observed only upon neurological examination in the emergency department and was not elicited on subsequent days. Transient nystagmus was noted by a nurse on the sixth day of hospitalization and had possibly been seen by the patient's wife before admission. A thiamine level was not obtained before treatment in our patient and is rarely assessed in the diagnosis of Wernicke's encephalopathy, which is generally a clinically based diagnosis.

FIGURE 1. Average Patient Weight Loss in the Months After Gastric Bypass Surgery[a]



[a] As of October 2004. Data courtesy of the Duke Health System Weight Loss Surgery Center, Duke Health Service, Duke University Medical Center.

Psychotic Disorder or Wernicke's Encephalopathy?

Persistent vomiting and rapid weight reduction after gastric bypass surgery are two consistently reported features in cases of Wernicke's encephalopathy in the medical literature since 1982 (14, 15, 27, 28). In 22 subjects with psychosis whose illness was summarized by Cirignotta et al. (14), the average daily weight reduction was 0.36 kg (range=0.11–0.66) (0.79 lb, range=0.24–1.45). All subjects persistently vomited. The average time from the surgery to the onset of psychosis was 93 days (range=21–365). Although our patient's weight at the onset of psychosis was not documented, his average daily weight reduction after gastric bypass surgery was calculated at 0.56 kg (1.23 lb). His weight reduction was therefore much higher than the average weight reduction after gastric bypass surgery (Figure 1). The onset of his psychosis occurred 52 days after gastric bypass surgery.

Thiamine deficiency is considered the cardinal cause of Wernicke's encephalopathy, which has been alleged to be the major cause of psychosis after gastric bypass surgery, and persistent vomiting is a prominent feature of Wernicke's encephalopathy after gastric bypass surgery. Although thiamine supplementation of 1.0–1.5 mg/day postoperatively is routinely suggested, patients with postoperative hyperemesis may require much higher doses or even parenteral supplementation (14, 29, 30). In general, parenteral supplementation of thiamine abates acute symptoms related to Wernicke's encephalopathy. In our patient, thiamine supplementation was not provided until hospitalization at our facility. Wernicke's encephalopathy was not initially included in differential diagnoses nor was the potentially significant role of hyperemesis (13). Our patient's psychotic symptoms were refractory to traditional psychopharmacological treatments and did not improve until the hyperemesis was corrected.

Mechanisms in addition to thiamine deficiency for Wernicke's encephalopathy or psychotic disorder after gastric bypass surgery may exist. Some authors implicate protein deficiency and "starvation injury" as etiological factors in psychosis after gastric bypass surgery (13). Our patient had a mildly decreased albumin level (30.0 mg/dl) that remained almost unchanged (31.0 mg/dl) after 7 weeks; his albumin level at admission was within normal limits but dropped to a low of 12.9 mg/dl before the dilation of the anastomotic stricture. Some authors suggest that rapid metabolism of lipids might be the cause of major nutritional deficits and/or the cause of encephalopathy (23). Our patient's total cholesterol level dropped from 250 mg/dl preoperatively to 112 mg/dl during his hospitalization. Despite many interesting theories, to our knowledge, there are no prospective studies regarding the underlying cause or mechanism of psychosis after gastric bypass surgery.

Patients who have received gastric bypass surgery or have other reasons for rapid weight reduction should be considered at risk for thiamine deficiency or Wernicke's encephalopathy. Although treatment with intramuscular or intravenous thiamine poses minimal risk to patients, delay of appropriate treatment with thiamine supplementation may result in a prolonged course of illness or death in patients who have Wernicke's encephalopathy. At the same time, focusing on Wernicke's encephalopathy as the only diagnosis of psychosis after gastric bypass surgery may lead the physician to overlook other potential causes of psychosis. In our patient, correction of hyperemesis and optimization of caloric and nutritional intake to restore his ideal weight, in addition to supplementation of thiamine, were correlated with resolution of his psychosis.

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The authors thank the residents, consultants, nutritionists, and nurses for their contributions to the care of this patient.

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