

Venlafaxine Pharmacobezoar Causing Intestinal Ischemia Requiring Emergent Hemicolectomy

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Introduction

Pharmacobezoars are an uncommon but potentially problematic manifestation of drug overdose. Diagnosed radiographically, endoscopically, intraoperatively, or postmortem, a bezoar is a mass of any form of unabsorbed material within the gastrointestinal tract. When they occur, they tend to form at anatomic strictures at any point between the esophagus and the rectum. They commonly occur in patients with prior abdominal surgery or altered GI motility. Besides obstructive and ischemic complications when impacted, pharmacobezoars can also cause prolonged toxicologic effects due to the retained drug mass.

Venlafaxine is a bicyclic phenylethylamine antidepressant that inhibits serotonin, norepinephrine, and dopamine reuptake in the CNS. Morbidity and mortality from venlafaxine overdose are typically from seizures and cardiovascular toxicity. We describe a novel case of massive overdose of extended-release (ER) venlafaxine

leading to obstructive pharmacobezoar formation at the ileocecal junction, with consequent bowel ischemia and necrosis requiring emergent hemicolectomy.

Case Report

A 28-year-old woman with a history of major depression was brought to the emergency room at midnight, 1 hour following an intentional overdose of her venlafaxine medication. Her parents found empty bottles of venlafaxine ER 37.5 mg tablets (300 count) and venlafaxine ER 150 mg tablets (100 count) filled 1 and 13 weeks prior to presentation, respectively. On arrival to the emergency department (ED), the patient was asymptomatic. Initial vital signs included a temperature of 36.8°C, blood pressure of 137/82 mmHg, heart rate of 78 beats/min, and respiratory rate of 18 breaths/min. Among her normal physical examination findings was a nontender abdomen with active bowel sounds. Her initial laboratory work-up, including a complete blood count and basic metabolic panel, was unremarkable. Acetaminophen and aspirin levels were negative.

The regional poison control center was contacted. Based on the patient's prescription fill dates, the specialist in poison information calculated a maximum probable dose of 10 g. To achieve a 10:1 activated charcoal to drug ratio, 100 g of activated charcoal was recommended, which the patient tolerated well. Since there was concern for drug-induced seizures, further gastrointestinal decontamination measures, including whole bowel irrigation, were thought to incur too much risk of aspiration.

While in the ED, by 5 h after ingestion, the patient had developed tachycardia to a heart rate of 130 beats/min and tremulousness that was treated with a total of lorazepam

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2 mg IV. After further consultation with the regional poison control center, the patient was admitted for observation for cardiac arrhythmias and seizures.

Twenty-eight hours after ingestion, the patient began complaining of sharp abdominal pain at the right lower quadrant. At this time, she also had mild anorexia and one episode of loose liquid stool with no bright red blood per rectum. The patient's vital signs included a temperature of 37.2°C, blood pressure of 130/95 mmHg, heart rate of 112 beats/min, and respiratory rate of 20 breaths/min. On physical examination, the patient had tenderness suprapubically and diffusely across the right lower quadrant. Although she exhibited mild voluntary guarding, no rebound was noted. The patient also had active bowel sounds. Repeat laboratory testing was significant for an elevated white blood cell count of 18.8×10^3 cells/ μ L. Otherwise, a repeat basic chemistry panel was normal as well as lactate which was measured to be 1.3 mmol/L. A CT scan of the abdomen and pelvis with oral and IV contrasts was obtained, which revealed "extensive scalloping of the wall of the entire right colon with air in the wall" and a large mass of tablets in the cecum (Figs. 1 and 2). The patient was emergently taken to the operating room for an exploratory laparotomy, given concern for suspected right bowel ischemia.

On laparotomy, surgeons found a thick-walled and edematous right colon with surrounding cloudy ascites and inflamed edematous tissue. Beyond the hepatic flexure, the colon was completely normal on inspection and palpation, as were the small bowel, uterus, gallbladder, and liver. A right colectomy with a primary hand-sewn anastomosis was performed. Following removal, the specimen was bivalved, revealing a loose conglomeration of over 80 white, round tablets with central umbilication in the cecum with surrounding necrotic cecal mucosa (Fig. 3).



Fig. 1 Axial view of abdomen and pelvis using CT demonstrating tablet bezoar with associated bowel pneumatosis



Fig. 2 Coronal reconstruction of a CT scan of the abdomen and pelvis demonstrating tablet bezoar at the ileocecal junction

The tablets were identified as venlafaxine ER 37.5-mg and 150-mg tablets (Upstate Pharma, LLC) by visual inspection, correlation to the patient's pharmaceutical distribution record, and comparison to published images [1]. No activated charcoal was visualized. Pathologic inspection of the specimen revealed an area of green-to-black ulcerated necrosis on the cecum and ascending colon measuring 13.7 by 9.2 cm with surrounding edematous mucosa. No colonic masses or perforations were noted.

During the remainder of her hospital stay, the patient recovered well with normalization of her vital signs, return of bowel function, and sufficient pain control. After a psychiatric evaluation, she was discharged home on postoperative day 4 with intensive outpatient psychiatric follow-up.



Fig. 3 Excised right colon and cecum demonstrating tablet bezoar with associated necrotic cecal mucosa

Discussion

Pharmacobezoars are potentially deadly. On occasion, they can cause bowel obstruction with resultant ischemia [2–4]. Additionally, these pharmaceutical concretions can cause sustained toxic effects through continued release of active ingredients.

Historically, medications causing pharmacobezoar formation include aspirin, antacids, iron, bulk laxatives, and ER products such as nifedipine and theophylline. The etiology of bezoar formation is multifactorial. Patients who have alterations in gastrointestinal anatomy or dysmotility are at risk. Medications may form bezoars when they modify gastrointestinal function. Anticholinergics and opioids slow gut motility. In overdose, aspirin is believed to cause pylorospasm, delaying gastric emptying. Pharmaceuticals, including extended- or sustained-release (SR) products, with significant unabsorbable components, are prone to bezoar formation. For example, nifedipine SR products consist of an insoluble cellulose acetate shell that is excreted whole [5]. Finally, massive tablet ingestions, regardless of formulation, have caused pharmacobezoars [6, 7].

Our patient developed a venlafaxine ER pharmacobezoar. Two factors from the patient's ingestion history, the massive quantity of tablets and the venlafaxine ER product's (Upstate Pharma, LLC) insoluble cellulose acetate shell, increased the risk of pharmacobezoar formation.

An unusual aspect of this case is the absence of overt clinical or radiographic signs of bowel obstruction despite development of bowel ischemia from a pharmacobezoar. There are two potential explanations. First, the patient likely had a partial or evolving bowel obstruction. Some degree of obstruction certainly existed for a bezoar to form at the anatomic stricture of the ileocecal junction. Additionally, the patient's concomitant loose stool while developing abdominal pain is consistent with encopresis. It may be that diagnosis and intervention occurred prior to complete bowel obstruction. A second explanation is that local drug effects contributed to the development of tissue ischemia. Theoretically, bowel wall immediately adjacent to a pharmacobezoar would be exposed to relatively high drug concentrations. Norepinephrine reuptake inhibition is already known to contribute to systemic toxicity from venlafaxine. High, local tissue concentrations of venlafaxine might cause focal alpha-adrenergic vasoconstriction. Such vasoconstriction could further compromise perfusion to tissue already under mechanical stress from the bezoar, worsening ischemia. In this case, we believe that our patient's bowel ischemia was primarily due to an evolving mechanical bowel obstruction, but possibly exacerbated by localized drug toxicity.

There have been only two case reports of venlafaxine overdose with gastrointestinal manifestations. First, a 47-year-old female who ingested an estimated 15 g of venlafaxine SR formed a gastric bezoar. The bezoar was diagnosed when high gastric residuals through the first 5 days of her hospital course warranted endoscopic investigation. The patient ultimately suffered devastating cerebrovascular infarcts from multiple seizures and hypoxia from respiratory arrest, aspiration pneumonitis, and acute respiratory distress syndrome [8]. Second, a 39-year-old female who ingested an estimated 30 g of venlafaxine capsules suffered from bowel ischemia and perforation due to persistent, refractory hypotension. On day 14 of her hospital course, bowel ischemia and perforation were diagnosed by rapid abdominal distention and intraperitoneal air visualized radiographically. No bezoar was found on emergent laparotomy [9]. In juxtaposition to these two cases, our patient was normotensive, although tachycardic, throughout her hospitalization and developed bowel ischemia from a venlafaxine pharmacobezoar diagnosed by exploratory laparotomy.

Effective screening for bezoars is difficult. Pharmaceuticals are inconsistently radio-opaque, so simple screening techniques such as abdominal X-rays would likely have poor sensitivity. Given the rarity of pharmacobezoars, it is difficult to justify the expense, resource utilization, and radiation exposure for routine endoscopy or CT scan in patients who exhibit no abdominal signs or symptoms. Therefore, we believe that diagnostic studies should continue to be reserved for patients with abdominal signs and symptoms.

Therapy for pharmacobezoars are numerous, but controversial. They include multiple-dose activated charcoal (MDAC), whole bowel irrigation (WBI), endoscopic removal, and surgical removal. For one, repeated doses of activated charcoal should absorb drug continually released from a retained pharmacobezoar, limiting further drug toxicity. However, since activated charcoal itself is unabsorbable, MDAC risks exacerbation of an existing pharmacobezoar or creation of a new one [2]. Another option, WBI has been utilized with inconsistent success to hasten passage or disruption of a pharmacobezoar [7–8]. If initiated early after a massive ingestion, WBI may prevent bezoar formation altogether. However, these potential benefits must be weighed against potential aspiration risks. And, in the setting of a complete bowel obstruction or ileus, bowel distention with liters of fluid is dangerous. Endoscopy is another potential intervention. Numerous successful reports exist for both gastric and colonic bezoars. As well, this method is not always successful and procedural complications, such as upper GI bleeding, have been reported [6].

Considered by most as an intervention of last resort, surgical removal of pharmacobezoars has been performed under select circumstances. Typically, intraoperative removal has been performed when a pharmacobezoar has caused frank or progressive bowel obstruction or has been refractory to more conservative treatment [10, 11]. Rarely, a pharmacobezoar causes bowel ischemia, necessitating emergent surgical intervention [2–4].

We describe a novel case of a venlafaxine ER bezoar causing intestinal ischemia necessitating emergent hemicolectomy. This case illustrates the need for clinical suspicion for pharmacobezoar formation in the setting of a massive extended-release pharmaceutical ingestion. In these circumstances, patients who have active bowel sounds and low risk for aspiration should be considered for multiple doses of activated charcoal and/or whole bowel irrigation. These therapies may mitigate prolonged toxicologic drug effects and prevent formation or hasten passage of a pharmacobezoar, respectively. Diagnostic endoscopy or CT scan should be reserved for patients exhibiting abdominal signs and symptoms.

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References

1. “Harrison’s practice—answers on demand.” *Harrison’s Practice | Drug Monographs*. <http://www.harrisonspractice.com/practice/ub/index/DrugMonographs/Drug_Monographs>. Accessed 01 Sept 2010.
2. Atkinson SW, Young Y, Trotter GA (1992) Treatment with activated charcoal complicated by gastrointestinal obstruction requiring surgery. *BMJ* 305:563
3. Korenman MD, Stubbs MB, Fish JC (1978) Intestinal obstruction from medication bezoars. *JAMA* 240(1):54–55
4. O’Malley JA, Ferrucci JT Jr, Goodgame JT Jr (1981) Medication bezoar: intestinal obstruction by an isocal bezoar. Case report and review of the literature. *Gastrointest Radiol* 6 (2):141–144
5. Prisant LM, Spaulding VC (2006) Antihypertensive pharmacobezoar. *J Clin Hypertens (Greenwich)* 8(4):296–298
6. Lapostolle F, Finot MA, Adnet F, Borron SW, Baud FJ, Bismuth C (2000) Radiopacity of clomipramine conglomerations and unsuccessful endoscopy: report of 4 cases. *J Toxicol Clin Toxicol* 38(5):477–482
7. Robert R, Frat JP, Veinstein A, Rouffineau J (2005) Protective effect of medication bezoar after a massive beta-blocker, digoxin, and amitriptyline poisoning. *Clin Toxicol (Phila)* 43 (5):381–382
8. Djogovic D, Hudson D, Jacka M (2007) Gastric bezoar following venlafaxine overdose. *Clin Toxicol (Phila)* 45(6):735
9. Mazur JE, Doty JD, Krygiel AS (2003) Fatality related to a 30-g venlafaxine overdose. *Pharmacotherapy* 23(12):1668–1672
10. Kwon HY, Scott RL, Mulloy JP (1996) Small bowel Procardia XL tablet bezoar mimicking cystic pneumatosis intestinalis. *Abdom Imaging* 21(2):142–144
11. Townsend CM Jr, Remmers AR Jr, Sarles HE, Fish JC (1973) Intestinal obstruction from medication bezoar in patients with renal failure. *N Engl J Med* 288(20):1058–1059