


Medication-Induced Gastroparesis: A Case Report

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M Ammar Kalas, MD¹, Gian Marco Galura, MD¹,
and Richard W. McCallum, MD, FACP, FCGP¹

Abstract

Gastroparesis is a commonly diagnosed gastrointestinal disorder with a high prevalence globally and high disease burden to those afflicted with it. Etiologies are variable with idiopathic and diabetes being the most common causes of gastroparesis. Management of gastroparesis depends on the etiology, and accurate diagnosis is required for better targeted therapy. Medication-induced gastroparesis is reversible, and discontinuing the medication is generally curative. This case report discusses 2 cases of medication-induced gastroparesis which were initially diagnosed as diabetic gastroparesis, and thorough history taking revealed the cause to be medication induced. Repeat studies following medication discontinuation revealed improvement in symptoms and resolution of gastroparesis. Further research needs to be done to assess the frequency of misdiagnosing diabetic patients with gastroparesis due to medications, specifically glucagon-like peptide-1 receptor agonists which are increasingly being used in diabetics.

Keywords

gastroenterology, gastroparesis

Introduction

Gastroparesis (GP) is a syndrome that commonly presents with abdominal pain, nausea, vomiting, and abdominal fullness in the absence of a mechanical obstruction. It has a prevalence of approximately 2.4 per 100 000 in the United States.¹ This syndrome has a higher predilection toward females with >70% of cases being females. These symptoms often led to poor quality of life, increased economic burden, increased clinic and emergency department visits, and hospitalizations.^{2,3} Etiology of GP can be due to diabetes mellitus (DM), idiopathic, postsurgical (eg, vagotomy), medications, and neurologic and systemic diseases.^{1,2} This report details 2 cases of drug-associated GP in a long-standing diabetic patient.

Case Presentation

The first case is that of a 52-year-old female with a long-standing history (10 years) of type 2 DM who was referred to our clinic for a 7-month history of postprandial epigastric pain, accompanied by fullness, bloating, and nausea. Multiple pharmacologies were tried to relieve the symptoms such as proton pump inhibitors and antispasmodics (anticholinergics), however with no relief. Laboratory tests and computed tomography of the abdomen were unremarkable. Patient had an HbA1c of 5.7% (well-controlled diabetes). Prior upper and lower endoscopies showed no evidence of obstruction,

and biopsy was negative for *Helicobacter pylori*. A hepatobiliary iminodiacetic acid (HIDA) scan was also done in the past which ruled out gallbladder dyskinesia, and an abdominal Doppler blood flow study ruled out median arcuate ligament syndrome. Upon extensive history taking, it was found that the patient had started semaglutide (a glucagon-like peptide-1 [GLP-1] receptor agonist) subcutaneous injection weekly, approximately 1 month prior to the onset of symptoms. A 4-hour scintigraphic gastric emptying study (GES) showed 24% retention of isotope in the stomach at 4 hours which indicates delayed gastric emptying (GE) as gastric residual remaining at 4 hours should be <10%. Semaglutide was subsequently held for 6 weeks with resolution of symptoms. A repeat GES was then performed and showed resolution of delayed GE (Table 1).

The second case is that of a 57-year-old female with a long-standing history (16 years) of type 2 DM presenting with abdominal bloating, nausea, and vomiting for the past

¹Texas Tech University Health Sciences Center, El Paso, USA

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Corresponding Author:

M Ammar Kalas, Department of Internal Medicine, Texas Tech University Health Sciences Center, 4800 Alberta Avenue, MSC 41107, El Paso, TX 79905, USA.

Email: Mkalas@ttuhsc.edu



Table 1. Gastric emptying study results.

Before stopping semaglutide 0.5 mg/SC weekly		
Time	Percentage retained	Normal values
1 hour	93%	<90% and >30%
4 hours	24%	<10%
After stopping semaglutide 0.5 mg/SC weekly for 6 weeks		
1 hour	77%	<90% and >30%
4 hours	6%	<10%

Table 2. Gastric emptying study results.

Before stopping dulaglutide 1.5 mg/SC weekly		
Time	Percentage retained	Normal values
1 hour	92%	<90% and >30%
4 hours	35%	<10%
After stopping dulaglutide 1.5 mg/SC weekly for 4 weeks		
1 hour	82%	<90% and >30%
4 hours	3%	<10%

year. Labs were significant for a HbA1C of 8.2%. Previous upper endoscopy and colonoscopy did not reveal any obstruction or other abnormalities; however, she never received a GES. In addition, patient started dulaglutide subcutaneous weekly injection (GLP-1 receptor agonist) approximately 15 months ago. A 4-hour scintigraphic GES showed 35% retention of isotope in the stomach at 4 hours, revealing delayed GE. Subsequently, dulaglutide was discontinued for 4 weeks with gradual resolution of symptoms. A repeat GES was then performed and showed normalization of GE (Table 2).

Discussion

Gastroparesis is a disease with variable presentations ranging from mild nausea and abdominal fullness to recurrent vomiting and abdominal pain symptoms.⁴ The diagnosis requires evidence of delayed GE based on a radionuclide study using an isotope-labeled solid meal for 4-hour duration in addition to the absence of mechanical obstruction. Hence, workup generally includes upper and sometimes lower endoscopies. Prolonged DM (>10 years) can cause GP due to neuronal damage which is irreversible and a result of prolonged uncontrolled blood glucose levels.^{3,4} Several medications such as proton pump inhibitors, anti-Parkinson's medications, illicit drugs (marijuana), opioids, and GLP-1 receptor agonists have been associated with delayed GE. It is crucial to identify causative drugs as discontinuation of the drug can result in resolution of the symptoms as seen in the 2 cases described above. However, in diabetics, it can be tricky owing to the fact that both diabetes and GLP-1 receptor agonists (an agent for diabetes management) can cause delayed GE; hence, the timeline of drug initiation and symptom onset becomes of the utmost importance. Glucagon-like peptide-1

receptor agonists act through the incretin receptors, which results in glucose-dependent insulin secretion and a decrease in glucagon release. Furthermore, GLP-1 receptor agonists inhibit the motility of the stomach antrum and the duodenum in addition to pyloric contraction which slows GE.⁵

Studies have proved that GLP-1 receptor agonists can cause delayed GE. It is thought that long-acting GLP-1 receptor agonists (weekly dosing primarily) are not associated with delayed GE due to tachyphylaxis and GE improvement upon continued use. In addition, GLP-1 receptor agonists are thought to be dependent on a baseline GE rate, and in patients with preexisting GP, they are thought to have minimal or no effect on GE.⁶ Furthermore, a prospective study done in 2020 evaluated the effect of GLP-1 receptor agonists weekly dosing over 8 weeks and showed evidence of delayed GE at 120 minutes at the end of 8 weeks. However, no GES was done during the study, and therefore, tachyphylaxis presence or absence cannot be concluded.⁷ Another double-blinded study in 2013 evaluated liraglutide daily dosing and its effects on 5-hour GES. Liraglutide was administered for a period of 5 weeks, and the study was significant for increased gastric retention at 1 hour which normalized between the liraglutide and placebo group at 5 hours.⁸

A study in 2010 was done to assess the effect of endogenous GLP-1 on GE and glucose levels. It compared healthy individuals receiving a GLP-1 antagonist with those on placebo and assessed their GE rates and the rise in blood glucose following oral intake. Individuals receiving the GLP-1 antagonists had accelerated GE when compared with those receiving placebo. In addition, the rise in blood glucose levels was more significant in patients on the GLP-1 antagonists.⁹ This study can be used to extrapolate the theory that the opposite, being that GLP-1 receptor agonists can cause delayed GE, is true.

The obesity pandemic has been on the rise, and according to the Centers for Disease Control and Prevention, the prevalence of obesity rose from 30.5% in 1999 to 2000 to 42.5% in 2017 to 2018.¹⁰ As the prevalence of obesity is rising, type 2 DM is also following a similar pattern. Glucagon-like peptide-1 receptor agonists are being prescribed more due to their dosing schedule and desired side effect of weight loss as a result of decreased GE and resultant early satiety, which in turn can help with diabetes control.

These 2 cases we present highlight the importance of history taking and making an accurate diagnosis of diabetic GP, an entity that is regarded as being irreversible, whereas medication-induced GP is reversible with medication discontinuation.

Authors' Note

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Declaration of Conflicting Interests

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Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed Consent

Verbal informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

ORCID iD

M Ammar Kalas  <https://orcid.org/0000-0002-6230-9172>

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