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Cannabinoid Hyperemesis Syndrome in a 23-Year-Old Woman with Uncontrolled Type 1 Diabetes Mellitus

Authors' Contribution:

Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Patient: Female, 23-year-old
Final Diagnosis: Cannabinoid hyperemesis syndrome
Symptoms: Intractable vomiting
Clinical Procedure: —
Specialty: Gastroenterology and Hepatology

Objective: Challenging differential diagnosis

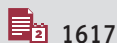
Background: Patients with type 1 diabetes mellitus may experience gastrointestinal symptoms, including those suggestive of diabetic gastroparesis. Cannabinoid hyperemesis syndrome (CHS) includes nausea, vomiting, and abdominal pain in the setting of chronic cannabinoid use. This report presents a case of CHS in a 23-year-old woman with uncontrolled type 1 diabetes mellitus.

Case Report: A 23-year-old woman with chronically uncontrolled type 1 diabetes mellitus had been presenting monthly at the emergency department for the last 2 years, for acute bouts of intractable nausea and vomiting, occasionally with abdominal pain. Given her history of uncontrolled diabetes, she had been managed for diabetic gastroparesis with prokinetics. A gastric emptying study 6 months prior to admission was normal, and the patient had had multiple unremarkable abdominal computed tomography imaging scans. On this admission, she benefited from supportive management with only temporary improvement of symptoms. On further questioning, she reported consistent use of cannabis for the last few years, and regression of acute vomiting with hot baths at home. With counseling, she ceased cannabis for 2 months and was symptom-free during this period.

Conclusions: This report has shown the importance of taking a comprehensive drug history in all patients, including in patients with type 1 diabetes, and is a reminder that cannabinoid use can cause severe nausea, vomiting, and abdominal pain in this patient group.

Keywords: Cannabis • Diabetes Mellitus, Type 1 • Gastroparesis • Intractable Vomiting

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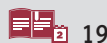
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Background

Diabetic gastroparesis (DGp) is delayed gastric emptying, in the absence of mechanical obstruction, that is attributable to diabetes mellitus (DM) [1,2]. It typically presents with postprandial fullness, nausea, vomiting, anorexia, and weight loss, with or without abdominal pain [1]. DGp is a debilitating disease associated with a poor quality of life, and constitutes a considerable financial burden on the United States health care system [3]. Up to 50% of patients with moderately controlled DM have delayed gastric emptying, and it is more common in patients with type 1 diabetes [4,5]. DGp has been used in the past to describe different clinical presentations, and was often used interchangeably with the term diabetic gastropathy [1]. In 1999, given that patients with this syndrome may have rapid gastric emptying, Koch et al defined diabetic gastropathy as a clinical condition presenting with upper gastrointestinal symptoms suggestive of an upper motility disturbance in patients with diabetes, whether or not delayed gastric emptying was present [6]. However, in August 2022, the American College of Gastroenterology (ACG) put forth guidelines recommending that for a definite diagnosis of gastroparesis to be made, delayed gastric emptying should be confirmed with a 4-hour gastric emptying scintigraphy test [7].

Cannabinoid hyperemesis syndrome (CHS) on the other hand, is a condition in which a patient experiences cyclical nausea, vomiting, and abdominal pain in the setting of prolonged cannabis use [8]. Bouts of episodic nausea and vomiting typically occur every few weeks to months and cease once the patient stops cannabis use [8,9]. An almost pathognomonic aspect of CHS is that symptoms are relieved with hot baths or showers. Seeing as DGp and CHS present with similar symptoms, when a patient with uncontrolled diabetes and chronic cannabis use presents with recurrent nausea and vomiting, this poses a diagnostic dilemma [10]. Since CHS was first described in 2004, several cases have been described. The largest case series of CHS to date reviewed 98 patients seen at the Mayo Clinic from 2005 to 2015 [11]. There was no mention of a history of diabetes in these patients, but gastric emptying studies had varying results, ranging from normal to slowed to rapid gastric emptying, making differential diagnosis with diabetic gastroparesis all the more challenging. Furthermore, cannabis use may be associated with an increased risk of diabetic ketoacidosis in patients with type 1 diabetes. This report presents a patient with type 1 DM who was diagnosed with CHS only after multiple presentations for intractable vomiting and abdominal pain, initially ascribed to DGp.

Case Report

A 23-year-old woman with a 7-year history of uncontrolled type 1 DM (A1c 8.8-16.5%; normal <5.7%), chronic kidney disease

stage 3, and cannabis use disorder, presented with intractable vomiting and abdominal pain for 3 days. She denied hematemesis, diarrhea, fever, or new medications. In the preceding year, she had been seen at the emergency department on a monthly basis with similar symptoms. She had benefitted from multiple sessions of computed tomography (CT) imaging of the abdomen, which were unremarkable. Six months prior to the present admission, she had an esophagogastroduodenoscopy, which was significant for esophagitis and a scintigraphic gastric emptying study, which showed normal gastric emptying. She was started then on as-needed metoclopramide for probable gastroparesis in the setting of uncontrolled diabetes.

On this admission, physical examination was pertinent for epigastric tenderness but normal vitals. Laboratory studies were pertinent for mild normocytic anemia at 11.2 g/dl (normal: 12-14 g/dl), normal lipase, hyperglycemia at 199 mg/dl (normal: 90-130 mg/dl) with serum bicarbonate of 26 mmol/l (normal: 22-29 mmol/l), serum creatinine 2.13 mg/dl (baseline creatinine, 1.4 mg/dl; normal: 0.59-1.04 mg/dl), and urine positive for cannabinoids. The initial impression was CHS. She received supportive management consisting of intravenous hydration, antiemetics, as well as intravenous Haldol with transient improvement of symptoms. Two days later, she complained of severe epigastric pain. A repeat CT scan and an additional hepatobiliary iminodiacetic acid (HIDA) scan were both normal. She improved with continued conservative management. At this point, considering her history of chronic cannabis use and unrevealing prior investigations, there was a greater concern for CHS. On taking further history, she reported marked improvement in symptoms after hot baths. She was smoking cannabis at least 5 times a week and her last use was 2 days prior to presentation. She was counseled on cannabis cessation and discharged on metoclopramide. Following discharge, she abstained from cannabis for 2 months during which she remained symptom-free until she restarted the use of cannabis and symptoms reoccurred. This 2-month period was the longest she had remained symptom-free.

Discussion

This report invites providers to broaden their differential diagnoses and think of CHS when faced with patients with recurrent nausea, vomiting, and abdominal pain, even when they have competing likely diagnoses such as diabetic gastroparesis.

Marijuana is the most commonly used federally illegal drug in the US and its use is up-trending. In 2019, 48.2 million people used it at least once [12].

CHS is characterized by stereotypical episodic hyperemesis usually with abdominal pain, in the setting of chronic cannabis

use [13]. The exact mechanism of CHS is not known; however, a few have been hypothesized. Cannabis is said to have a biphasic effect, with low doses conferring an antiemetic effect but persistent high dose ingestion resulting in vomiting due to derangement of the endocannabinoid system [9]. Since it was first described in 2004 [14], several case reports and case series have been published; however, its exact prevalence is unclear, owing to the fact that, due to the illegal nature of the drug, patients do not always own up to its use [8]. Also, it still represents a diagnostic challenge and is often not recognized by health care providers [15]. This often results in multiple emergency department visits and hospital admissions prior to diagnosis [15], especially when patients are diabetic [10]. In 2020, Aung et al published a case series of 4 patients with type 1 diabetes who were diagnosed with CHS only after a minimum of 12 admissions, with a total time to diagnosis ranging from 2 to 13 years [10]. During this time, they had each undergone multiple imaging, laboratory, and endoscopy studies, some which were repeated more than once. This is similar to what happened with our patient. She had a history of chronically uncontrolled type 1 diabetes, and was diagnosed with CHS after almost 2 years of recurrent hospital admissions for the same upper gastrointestinal symptoms. She had had multiple CT imaging scans of her abdomen and repeated lab testing during this period. Our patient did have a gastric emptying study, which was normal, 6 months prior to when we made the final diagnosis. This helped guide us away from diabetic gastroparesis as the most likely diagnosis, given the current definition of gastroparesis [7]. However, we must say that a delayed gastric emptying in a patient with diabetes does not rule out CHS. In 2012, one of the largest case series of CHS by the Mayo Clinic [11], which included 98 patients meeting the criteria for CHS, showed that patients with CHS could have various findings on gastric emptying analysis: 30% of patients had delayed gastric emptying, 25% had rapid emptying, and 46% had normal emptying. Several diagnostic algorithms have been proposed for the diagnosis of CHS [11,16,17]. The most known among these is the Rome IV criteria [18]. According to Rome IV, required criteria for the diagnosis of CHS include: i) stereotypical episodic vomiting resembling cyclic vomiting syndrome in terms of onset, duration, and frequency; ii) presentation after prolonged, excessive cannabis use; iii) relief of vomiting episodes by sustained cessation of cannabis use. These criteria must have been fulfilled for the last 3 months and symptom onset must have been >6 months for the diagnosis to be

made. Our patient met all these criteria as she had been presenting monthly to the ED for intractable nausea and vomiting, she had reported an 8-year history of frequent cannabis use, and she remained symptom-free for 2 months (the longest period without symptoms for her) once she temporarily ceased cannabis use.

Some authors have expressed the concern that the Rome IV criteria may be too restrictive and therefore miss a considerable number of patients who effectively have CHS. They have thus enlarged the diagnostic criteria to include temporary relief of symptoms with hot bathing and abdominal pain accompanying the severe cyclic vomiting [19]. Our patient did meet these criteria as well.

The differential diagnoses for vomiting and abdominal pain in patients with type 1 diabetes, however, remain overwhelmingly broad. For our patient, DGp appeared unlikely. Normal lipase had helped ruled out pancreatitis. A normal CT abdomen and HIDA scan ruled out bowel obstruction and cholecystitis, respectively. We had thought of diabetic ketoacidosis, but she was not acidotic. She had no fever or diarrhea which would point to an infectious cause. Her recent esophagogastroduodenoscopy had ruled out a gastric outlet obstruction. She was not on any medication that would lead to vomiting. Her electrocardiogram and troponin levels were not suggestive of an acute coronary syndrome. CHS appeared the most likely explanation at that time.

Conclusions

With the legalization of cannabis in the United States, clinicians can anticipate to encounter more and more patients presenting with complications of cannabis use. This report has shown the importance of taking a comprehensive social history in all patients, including in patients with type 1 diabetes, and is a reminder that cannabinoid use can cause severe nausea, vomiting, and abdominal pain in this patient group.

Physicians should always inquire about frequency of cannabis use. Moreover, relief of symptoms with cannabis cessation or hot baths should further heighten suspicion of CHS. This will help avoid unnecessary repeated tests and imaging and help initiate definite treatment much earlier.

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