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CASE REPORT | COLON

Rare Case of Endoscopically Diagnosed Ischemic Colitis Secondary to Chronic Phentermine Use

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ABSTRACT

Phentermine is an amine anorectic that acts as a sympathomimetic agent and undergoes hepatic metabolism predominantly through CYP3A4. It is commonly used as a mediation to facilitate weight loss. Side effects of phentermine can include pulmonary hypertension, valvular heart disease, palpitations, increased heart rate or blood pressure, diarrhea, and cognitive impairment. Very rarely, phentermine usage has been associated with causing ischemic colitis. The mechanism of action for ischemic colitis from phentermine is not well defined but will be discussed in this review. We present a case of a woman who used phentermine daily for weight loss and was endoscopically confirmed to have ischemic colitis after presenting with abdominal pain and bloody diarrhea.

KEYWORDS: ischemic colitis; phentermine; weight loss; medication side effects; single-stripe sign; endoscopy

INTRODUCTION

Phentermine is an amine anorectic that acts as a sympathomimetic agent and undergoes hepatic metabolism predominantly through CYP3A4.[1] It has been utilized as a pharmacotherapy agent for facilitating weight loss since the 1950s and was approved by the Food and Drug Administration in 2012.[2] Side effects of phentermine can include pulmonary hypertension, valvular heart disease, palpitations, increased heart rate or blood pressure, diarrhea, and cognitive impairment.[2,3] Thus far, there has been only 5 reported cases of phentermine-induced ischemic colitis published.[1,4,10,11,12] The mechanism of action for ischemic colitis from phentermine is not well defined but will be discussed in this review. We present a case of a woman who used phentermine daily for weight loss and was endoscopically confirmed to have ischemic colitis after presenting with abdominal pain and bloody diarrhea.

CASE REPORT

A 48-year-old woman with a history of Graves disease requiring thyroidectomy and hypertension presented to the emergency department due to abdominal pain and syncopal episode. Per the patient, she began to feel diaphoretic with abdominal pain while coming out from the bathroom at work and, subsequently, lost consciousness for 1 minute with mild confusion on awakening. She has never had a syncopal episode before. Symptoms after the event included severe transient crampy left upper quadrant abdominal pain and watery bowel movements with bright red blood. She denied any fevers, chills, nausea, or vomiting and endorsed drinking her normal amount of fluid daily. She had no recent travel history, sick contacts, or new food intake. The patient had no history of prior or current nonsteroidal anti-inflammatory drug use or over the counter supplements and denied smoking or illicit drug use. Family history was significant for colon cancer in her father diagnosed at the age of 39 years and in her cousin at the age of 43 years. The patient had a colonoscopy 3 years ago that was unremarkable; however, a prior 6-year colonoscopy revealed benign polyps.

On presentation to the emergency department, her vital signs were hemodynamically stable with a blood pressure of 147/83 mm Hg and no tachycardia, tachypnea, hypoxia, or febrile episode. Physical examination revealed mild distress, soft nondistended abdomen with tenderness-to-superficial and deep palpation in the left upper quadrant, no guarding or rigidity, and presence of bowel sounds. Her skin was warm, dry, and pink, and she was alert and cooperative. Laboratory workup was significant for hypokalemia of

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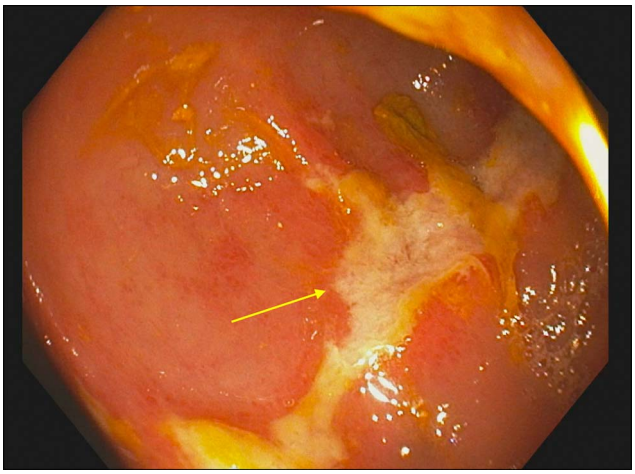

Figure 1 Arrow depicting long-linear ulcer at 35 cm from the anal verge extending to the descending colon with pale and uninvolved mucosa around the ulcer, representing a single-stripe sign.

3.5 mmol/L and normal blood urea nitrogen of 12 mg/dL and creatinine of 0.8 mg/dL, indicating no sign of intravascular volume depletion. Her amylase, lipase, liver enzymes, and bilirubin were within normal limits. She had an elevated high-density lipoprotein of 76 mg/dL and triglyceride 202 mg/dL, and negative beta-HCG. Her hemoglobin was within normal limits of 12.6 g/dL. The stool culture was negative for clostridium difficile, fecal ova and parasite, shigella, campylobacter, and salmonella. A computed tomography angiography of the abdomen and pelvis revealed mural thickening and luminal narrowing with infiltration of fat planes in the distal transverse colon, splenic flexure, and descending colon, which were findings consistent with colitis. She was treated symptomatically with fluid resuscitation, pain management, and a clear liquid diet. Owing to further episodes of bright red blood per rectum overnight, the patient was scheduled for a flexible sigmoidoscopy which revealed colitis with a long-linear ulcer at 35 cm from the anal verge extending to the descending colon

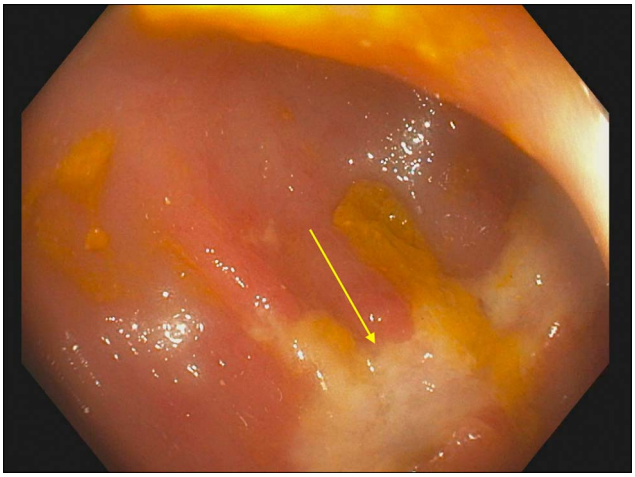

Figure 2 Arrow depicting long-linear ulcer at 35 cm from the anal verge extending to the descending colon with pale and uninvolved mucosa around the ulcer, representing a single-stripe sign.

with pale and uninvolved mucosa around the ulcer. This endoscopic appearance, as seen in Figures 1 and 2, was consistent with the colon single-stripe sign, which represents a single line of erythema with erosion or ulceration that is highly suggestive of ischemic injury.[13] Multiple cold-forceps biopsies were taken; however, the procedure was advanced to the descending colon with solid stool limiting further advancement.

The patient was started on empiric antibiotic therapy with intravenous piperacillin-tazobactam, and abdominal examinations were monitored closely for any worsening of pain, requiring a surgical consultation. Pathology results from the biopsies of the sigmoid colon revealed fragments of benign colonic mucosa with erosion and stroma hyalinization, suggestive of ischemic bowel disease. All other stool culture results and ova and parasites returned negative. The diagnosis was discussed with the patient, and her home medications were reviewed to determine a possible cause of ischemic colitis. She takes 40 mg of valsartan daily and has been taking phentermine 37.5 mg tablets daily for over 1 year to help with weight loss. In total, she has lost 12 pounds while on phentermine. On literature review, phentermine has been associated with ischemic colitis, and all other possibilities causing her diagnosis were ruled out. The patient's symptoms of abdominal pain and blood per rectum had subsided, and she was deemed stable for discharge on oral amoxicillin-clavulanic acid for a 5-day course. She was instructed to discontinue phentermine and follow-up with her physician outpatient.

DISCUSSION

Phentermine is a sympathomimetic amine that predominantly increases levels of norepinephrine and dopamine and serotonin from the hypothalamus in the central nervous system. The resulting increase in sympathetic stimulation is attributed for its usage as an appetite suppressant.[5] As mentioned previously, phentermine is one of the most prescribed medications for obesity treatment in the United States and has been approved by the Food and Drug Administration for short-term use of 12 weeks as an adjunctive therapy in patients with body mass index greater than or equal to 30 or 27 kg/m^2 with related comorbidities.[2] Little has been documented about the mechanism of phentermine causing ischemic colitis; however, the presumed pathophysiology can be extrapolated from the data on cocaine-induced ischemia.

There are 3 causal factors for cocaine-related ischemia including arteriolar vasospasm, platelet activation, and accelerated atherosclerosis.[14] The intestinal vasculature has adrenergic receptors stimulated by norepinephrine, leading to intense mesenteric vasoconstriction and tissue ischemia. Cocaine use leads to increased levels of norepinephrine in the synaptic cleft, thus increased risk for vasospasms.[14] Similarly, phentermine is an amphetamine derivative and, consequently, has similar systemic effects to them.

Amphetamine-induced systemic effects have been linked to increased norepinephrine in the peripheral nervous system and could lead to splanchnic vasoconstriction and smooth muscle hyperactivity, followed by potential watershed ischemia leading to ischemic colitis.[6–9]

To further support the association between phentermine and ischemic colitis, a case published in 2016 presented a 36-year-old woman with acute, severe abdominal pain accompanied by rectal bleeding. A computed tomography demonstrated marked mural thickening of the distal transverse, descending, and sigmoid colon consistent with infectious or inflammatory colitis without signs of obstruction or free air. A subsequent colonoscopy revealed extensive inflammation, edema, and necrotic membrane from the descending colon into the transverse colon. No clear etiology was found, but further questioning prompted the patient to reveal that she had taken 37.5 mg of phentermine daily for the past 2 years.[4] This was believed to be the culprit, and she was educated on discontinuation. A similar case in 2003 detailed a 59-year-old, obese woman who presented with rectal bleeding and suprapubic abdominal pain. Her medical history was unremarkable for risk factors of bowel ischemia. However, she had been taking phentermine 15 mg for 10 weeks, resulting in intentional weight loss of 12 kg. Colonoscopy demonstrated pathology associated with ischemic colitis and chronic ischemic morphological features, such as fibrosis.[10]

Given that phentermine is a commonly prescribed medication for the common diagnosis of obesity, it is important that rare side effects be discussed and shared. This potential for ischemic colitis should be made aware to all clinicians and considered when a patient is presenting with abdominal pain and associated gastrointestinal bleeding. Phentermine should be discontinued on presentation and further avoided, and use of other agents for weight loss should be discussed. We also suggest the completion of a follow-up endoscopy to assess for a healed colon after discontinuing phentermine.

Despite the wide usage of phentermine for assistance in weight loss, there have been minimal severe side effects reported. The rarity of ischemic colitis secondary to phentermine can be a potential life-threatening event that clinicians should be aware of in patients presenting with concerning symptoms who have been recently taking phentermine. We recommend completion of a detailed history and review of current medications to rule out other causes of ischemic colitis. Further evaluation with endoscopy and biopsy would be beneficial to confirm the diagnosis of ischemic colitis, and patients should be counseled on immediate cessation of phentermine and monitored closely.

DISCLOSURES

Author contributions: T. Nagi wrote the original manuscript and is the article guarantor. All authors reviewed and provided revisions to the manuscript.

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