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SARS-CoV-2 Enteritis in a Patient with a History of Roux-en-Y Gastric Bypass

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Abstract

As SARS-CoV-2, the virus responsible for COVID-19 disease, continues to spread rapidly, clinicians face an increasing heterogeneity in the presenting symptoms associated with active infection. In particular, digestive symptoms appear to be more common than previously thought with growing evidence suggesting that SARS-CoV-2 serves as a direct enteric pathogen. We report the first case of COVID-19 manifesting as radiographic and endoscopically-proven enteritis in a female patient with a history of Roux-en-Y gastric bypass. This report details the clinical presentation, radiographic and endoscopic findings, and real-time PCR tissue and stool sample analyses and thus represents one of the best-characterized cases of COVID-19 within the gastrointestinal tract to date. These findings not only add to the growing body of literature describing the myriad of COVID-19 manifestations, but also offers insight into mode of transmission and may help direct future health policy as well as scientific investigations.

Introduction

SARS-CoV-2 is the positive-sense single-stranded RNA virus responsible for the COVID-19 pandemic sweeping across the globe. Much like the previously characterized SARS-CoV virus, SARS-CoV-2 utilizes the ACE 2 receptor for cell entry[1, 2]. This receptor is highly expressed in respiratory epithelium as well as the small intestine and colon. While initial studies focused on respiratory manifestations, extra-pulmonary involvement is an active area of research. Initial population-based studies from China demonstrated a higher prevalence of gastrointestinal (GI) symptoms in patients than previously reported[3-5]. A recent review of the literature showed gastrointestinal symptoms are common, with a range in prevalence from 3 to 40.7 percent [6]. While the majority of GI symptoms are mild to moderate, more severe manifestations of COVID-19 have been published with a case report describing hemorrhagic colitis on endoscopy in a COVID-19 positive patient [7]. This suggests a direct causal relationship between SARS-Co-V2 and gastrointestinal infection although this has not been definitively proven in-vivo. Nevertheless, this has important implications regarding spread of disease with a growing body of evidence suggesting possible fecal-oral transmission[8-10].

Further studies are needed to better characterize the GI manifestations of COVID-19 and demonstrate their clinical significance and frequency. We present a case of suspected SARS-CoV-2 enteritis in a patient with a history of Roux-en-Y gastric bypass. The patient underwent radiographic and endoscopic evaluation along with quantitative rT-PCR evaluation of stool and tissue biopsy samples. To our knowledge, this represents the most comprehensive

diagnostic and clinical characterization of SARS-CoV-2 infection within the gastrointestinal tract to date and offers important insight regarding the infective nature of the virus, evolving clinical manifestations of the disease, as well as implications for future public health policy.

Case Report

On March 27, 2020, a 44-year-old woman recently diagnosed with COVID-19 on March 22, 2020, presented to the emergency department with a 3-day history of inability to tolerate oral intake with severe nausea, nonbilious vomiting and diarrhea. Her history was significant for hypertension, diabetes mellitus, chronic obstructive pulmonary disease (COPD), gastroesophageal reflux disease (GERD), obesity and bipolar disorder. She had a surgical history notable for Roux-en-Y gastric bypass 6 months prior to presentation and a negative diagnostic laparoscopy for chronic abdominal pain one month prior to presentation.

On further questioning, she denied a personal or family history of gastrointestinal disease. Her medications included Amlodipine, Losartan-Hydrochlorothiazide, Pantoprazole, Famotidine, Carafate, Seroquel, and Gabapentin. She denied antibiotic, antidiarrheal, and non-steroidal anti-inflammatory use, food allergies, lactose intolerance, alcohol abuse, nicotine use. She endorsed occasional marijuana use. She denied travel history but reported COVID-19 contacts in her apartment building.

The physical exam revealed a body temperature of 98.2, blood pressure of 132/98 mmHg, pulse of 91 beats per minute, respiratory rate of 21 breaths per minute, and oxygen saturation of 100% on ambient air. Lung auscultation was normal, and her abdominal exam demonstrated tenderness in the epigastrium.

Laboratory evaluation revealed an elevated white blood cell count of 13, with elevated neutrophils and normal lymphocyte and eosinophil distributions, a normal hemoglobin, and a C-reactive protein of 39.2 mg/dL. CT scan of her abdomen and pelvis with intravenous and oral contrast demonstrated a 20-centimeter segment of submucosal edema and mural thickening with stratified enhancement of small bowel distal to her gastrojejunostomy, consistent with enteritis (Figure 1).

She was admitted to a COVID isolation ward with respiratory and droplet precautions. Intravenous Ceftriaxone and Metronidazole were started for small bowel enteritis as well as intravenous proton pump inhibitor for suspected marginal ulcer. Before administration of antimicrobials, a fecal sample was obtained and was negative for stool culture of the following pathogens: Campylobacter, Salmonella, Shigella, Shiga-toxin producing E. coli and Yersinia, ova and parasites and Clostridium difficile toxin. Blood cultures were also negative. Additional work up included a normal upper gastrointestinal series with small bowel follow through. Endoscopy was deferred given the overall high-risk aerosolizing procedure in a known COVID-19 patient.

Over the next 3 days, the patient continued to have diarrhea and minimal oral intake. Two repeat nasopharyngeal swabs 24 hours apart were negative for COVID-19. She was thus considered COVID resolved and isolation precautions were removed. On hospital day 5, given her persistent abdominal pain and diarrhea, endoscopy was performed which confirmed viral enteritis within a 30-centimeter(cm) segment of jejunum approximately 20cm distal to her gastrojejunostomy. Additionally, the patient had a 1 by 1cm clean-based marginal ulcer. Several tissue biopsies from the ulcer and inflamed jejunum were obtained. Quantitative rT-PCR analysis of tissue biopsy samples was negative for SARS-CoV-2.

On hospital day 6, the patient developed a low-grade fever to 100.2 F. Given the endoscopic findings concerning for active intestinal infection and concerns for persistent viral shedding in stool, the patient was again placed on COVID isolation precautions. Total parenteral nutrition was initiated given her persistent poor oral intake in the setting of an anastomotic ulcer and enteritis. Over the course of the next few days the patient's symptoms improved. She was deemed safe for discharge with home TPN on hospital day 11. Stool samples were unable to be collected during this time.

The patient was readmitted April 16, 2020 for treatment of a right upper extremity deep venous thromboembolism and work up for persistent diarrhea. A repeat COVID-19

test was negative. A stool sample was obtained during this admission given her persistent diarrhea for rT-PCR analysis and was also negative for SARS-CoV-2. Her symptoms and oral intake improved and she was subsequently discharged home without TPN on hospital day 7.

Discussion

This detailed patient presentation and work up provides one of the best-characterized examples of gastrointestinal COVID-19 infection to date and highlights several important caveats to the evolving COVID-19 crisis. The constellation of findings presented here offer additional evidence for the direct infective capacity of SARS-CoV-2 within the GI tract resulting in clinically significant enteritis as seen on CT scan and endoscopy in the setting of an otherwise negative infectious workup. While quantitative rT-PCR samples of intestinal epithelium and stool were negative at time of sample acquisition, this does not definitively rule out SARS-CoV-2 as a direct enteric pathogen but rather a potential failure to capture the most active replication window or to sample tissues capable of sustaining viral replication. In vitro viral invasion studies support direct infection of intestinal epithelium by SARS-CoV-2, however, these experiments utilize uninflamed tissues[11]. Similarly, in vivo studies demonstrate viral replication and nucleocapsid protein staining in the intestinal samples from a series of SARS patients during the 2003 outbreak[12] and a single COVID-19 patient[13]; however, all tissue samples revealed histologically normal epithelium at time of biopsy. In fact, animal models demonstrate a significant downregulation in the ACE2 receptor as early as four days following onset of active inflammation[14]. Therefore it is possible that actively inflamed tissues are resistant to further viral invasion or sustained viral replication whereas healthy tissues support these events.

Both viral RNA as well as fecal nucleic acid can be isolated in the stool and on rectal swabs of COVID+ patients[13, 15, 16] and remain positive up to 14 days after negative nasopharyngeal swabs[9, 17]. Studies from 2003 confirmed SARS-CoV RNA was present and remained infectious within sewage water for up to 2 weeks and more recent studies suggest a similar environmental stability of SARS-CoV-2[18-20]. Taken together, these findings are highly suspicious for fecal-oral transmission and suggest that people with digestive symptoms represent a cohort of patients at particular risk of spreading the disease, even in the setting of negative respiratory samples [21]. This has led many clinicians to recommend routine rT-PCR testing of both stool and respiratory samples in patients with suspected COVID-19 disease. As more studies confirm the direct infective capacity of SARS-CoV-2 within the GI tract, it seems likely that fecal-oral transmission is an important route by which the disease spreads. It is imperative that in vivo testing of both inflamed and normal tissue be undertaken and stool testing kits be developed and disseminated such that hospital and public health policies can be adjusted accordingly.

The patient presented here underwent a Roux-en-Y gastric bypass several months prior to infection with COVID-19 and was on chronic proton-pump inhibitor therapy to prevent marginal ulceration. Studies have shown that coronaviruses are able to invade gastric epithelium and produce live virions at a more neutral pH[22][2]. This has led some to hypothesize that conditions which alter the gastric pH (i.e. helicobacter pylori infection, atrophic gastritis, and anti-secretory medications) may play a role in disease pathogenesis and increase one's risk for fecal-oral transmission[23][2]. An increased gastric pH along with a decreased gastric reservoir as seen following bariatric surgery may impair one's ability to decontaminate compromised food and thus increase the risk for gastrointestinal infection. This hypothesis was supported by a recent study by Almario and colleagues which showed a dose-response relationship between the use of antisecretory medications and COVID-19 positivity [24]. Further studies examining this possible association are needed for more definitive conclusions.

This report is the first to describe enteritis as a manifestation of COVID-19 in a patient following Roux-en-Y gastric bypass. It adds to the growing body of literature implicating the gastrointestinal tract in the clinical expression and transmission of COVID-19 and identifies a potential high-risk patient population for SARS-

Figure 1. CT scan of abdomen and pelvis in coronal (A) and axial (B) views demonstrates a long segment of small bowel with submucosal edema and mural thickening within the midabdomen consistent with enteritis.

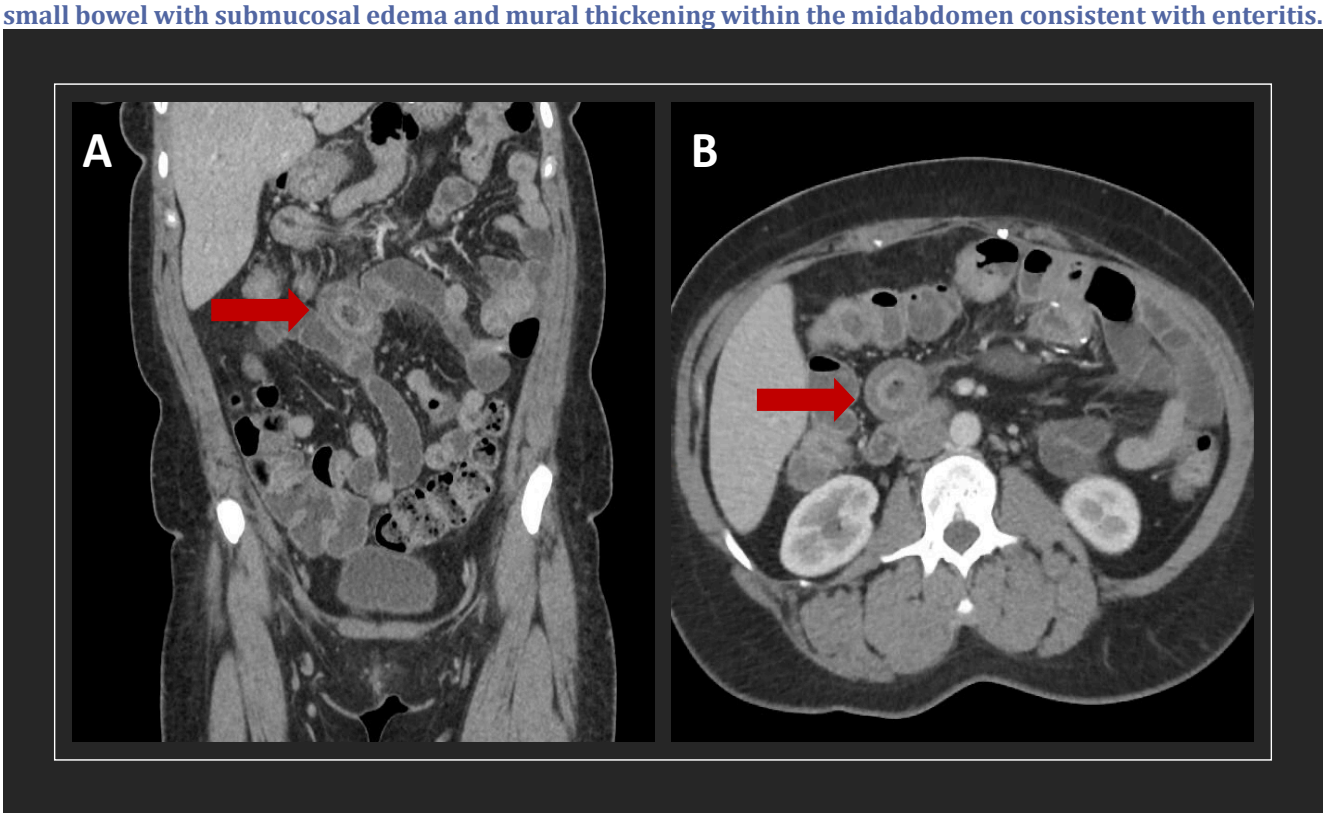
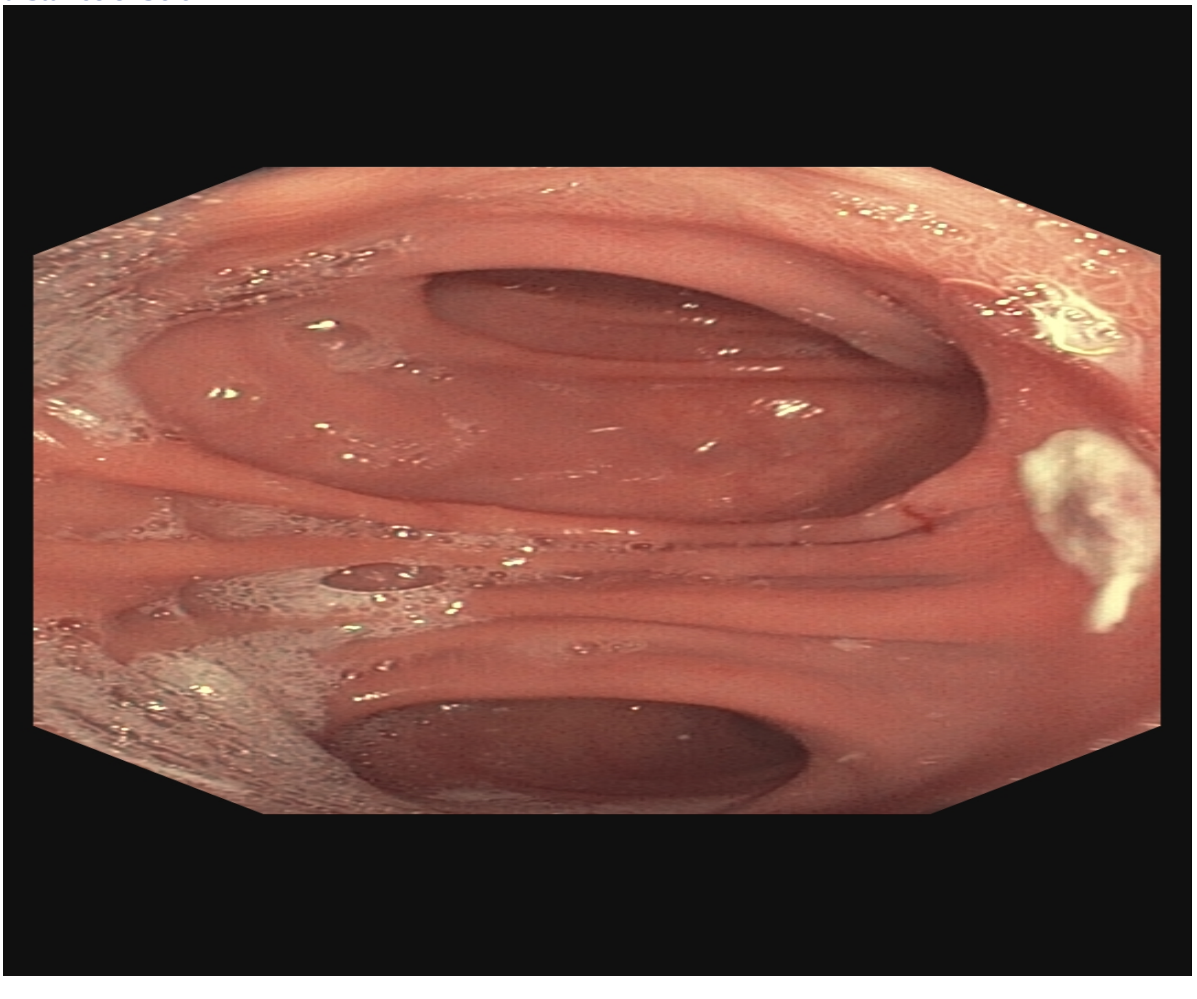


Figure 2 and Figure 3. Colonoscopy images showing a clean based 1x1 cm marginal ulcer and mild patchy erythema and hyperemia without ulceration or severe denudation 20 cm distal to the GJ anastomosis for a distance of 30 cm.



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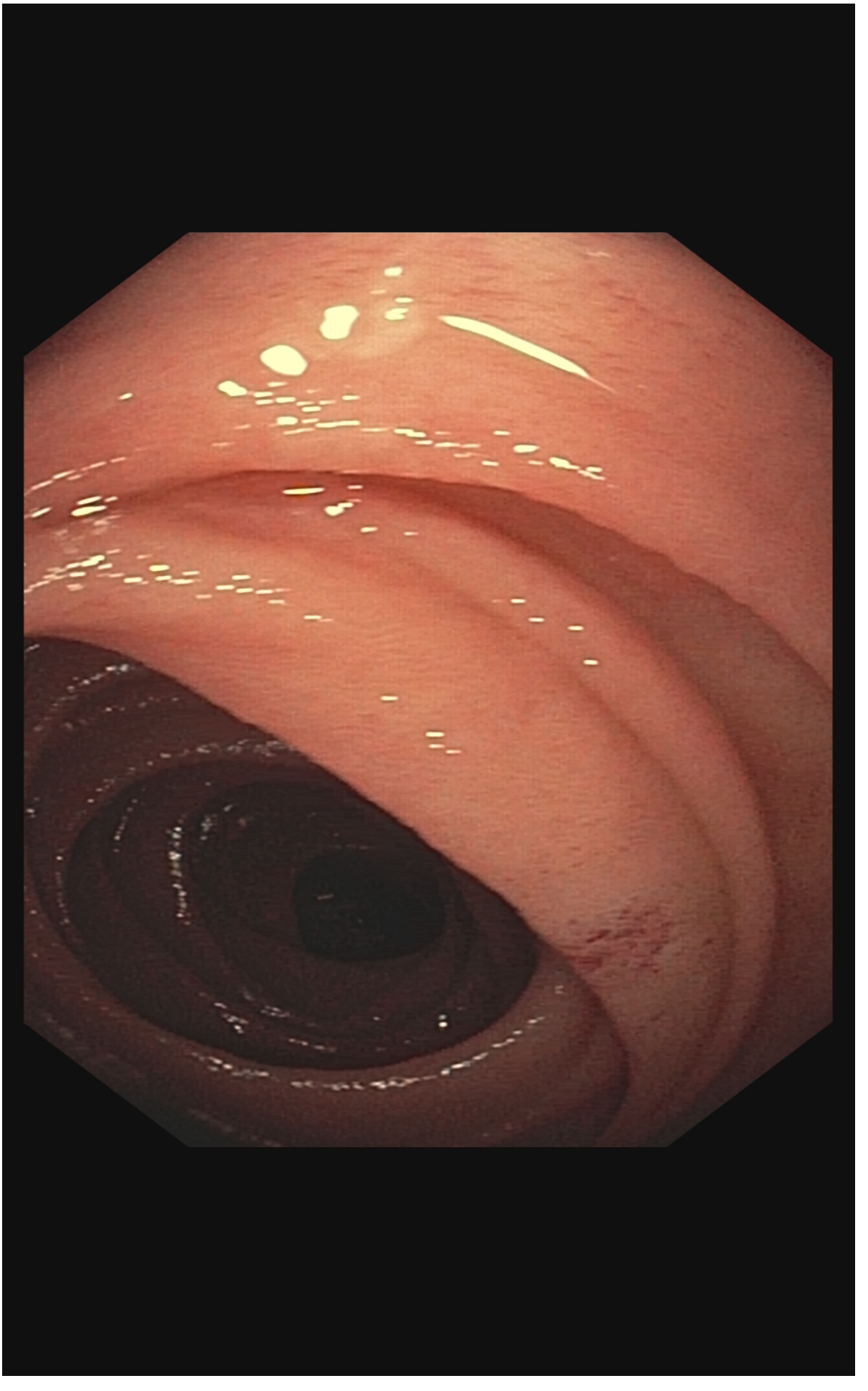

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