CASE REPORT CRSLS

A Late Presentation of COVID-19 Induced Bowel Ischemia

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ABSTRACT

Introduction: Infection with COVID-19 may lead to extrapulmonary pathologies secondary to the systemic inflammatory effects of the virus.

Case Description: This case report discusses a 55-year-old female patient who presented with small bowel obstruction (SBO) several months after resolution of a COVID-19 infection. The patient was surgically treated with a small bowel resection, and eventually made a full recovery.

Discussion: The pathophysiology of COVID-19-induced SBO can be explained by the prolonged inflammation and coagulation activation in the bowel's vasculature system. Under these circumstances, microthrombosis occurs in the bowel's microvasculature; the affected intestinal tissue becomes ischemic and infarcted. The damaged bowel is eventually replaced with fibrotic scar tissue, thus promoting bowel stricture and subsequent obstruction.

Conclusion: COVID-19 can be responsible for both acute and chronic embolic and thrombotic events in the mesenteric vasculature, which acts as a risk factor in the manifestation of SBO.

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INTRODUCTION

COVID-19 has systemic effects besides the pulmonary manifestations that are the hallmark of infection. There have been multiple reports in the medical literature documenting bowel ischemia and especially superior mesenteric thrombosis.[1–3] These reports describe acute thrombosis secondary to COVID-19, but there is a lack of data on the chronic effects of the disease.[4] We report a case of late presentation of bowel ischemia and stricture in a patient with a history of COVID-19 infection.

Case Presentation

The patient is a 55-year-old female with a history of a bilateral tubal ligation, robotic assisted hysterectomy with bilateral salpingo-oophorectomy for uterine fibroids, and a family history of ovarian cancer in the patient's mother. The patient was diagnosed with COVID-19 by reverse transcription polymerase chain reaction in June 2020. She did not require hospitalization. She had no loss of taste or smell, and no respiratory symptoms. During quarantine for COVID-19, the patient developed intermittent melena without abdominal pain. The patient's stool tested positive for occult blood. At this time the patient was not taking blood thinners nor nonsteroidal anti-inflammatory drugs. This persisted for several months. Due to the pandemic, she was unable to have a face-to-face physician visit, nor be seen by a gastroenterologist immediately. Eventually, she was seen by her gastroenterologist after her melena had ceased. The gastroenterologist performed an outpatient workup that included an upper gastrointestinal (GI) endoscopy toward the end of 2020, which was normal except for a hiatal hernia. The patient then developed acholic stools and an outpatient colonoscopy in 2021 demonstrated diverticulosis.

Approximately one year after her initial COVID-19 diagnosis, the symptoms progressed, and the patient was admitted to the hospital with crampy abdominal pain mostly localized to the epigastric and right upper quadrant. She also had nausea and emesis. The patient's labs were within normal

limits with aspartate aminotransferase: 27, alanine aminotransferase: 23, and total bilirubin: 00.7. The patient underwent a right upper quadrant abdominal ultrasound that demonstrated cholelithiasis and a positive sonographic Murphy's Sign. A computed tomography (CT) scan of the abdomen and pelvis demonstrated cholelithiasis and distended gallbladder; there was no evidence of gallbladder wall thickening or pericholecystic fluid (see **Figure 1**). Patient then underwent an uneventful laparoscopic cholecystectomy during her admission. Pathology revealed mild chronic cholecystitis with cholelithiasis. The patient was discharged the same day of her cholecystectomy feeling better.

Unfortunately, the patients' symptoms recurred and progressed over the subsequent weeks. She was admitted to the hospital three times in one month for recurrent partial small bowel obstruction (SBO). The patient underwent a CT abdomen and pelvis with contrast. The CT showed dilated loops of small bowel with a probable transition point at the midline pelvis; however, a precise location of the stricture could not be identified. This finding was concerning for a developing SBO. Most of the colon was relatively decompressed. No pericolonic inflammatory stranding was seen. There were multiple colonic diverticula without evidence to suggest acute diverticulitis. There was a small ventral anterior abdominal wall defect containing some fat. These findings were not appreciated on prior CTs.

She was managed nonoperatively each time. She reported a 40-pound weight loss in two months after the surgery. Approximately six weeks after surgery, she underwent upper endoscopy and lower endoscopy due to her persistent symptoms. She had focal gastritis and diverticulosis. Of note, the terminal ileum was intubated; about 30 cm of distal small bowel was examined and found to be grossly and pathologically normal. Patient was discharged home upon resolution of symptoms.

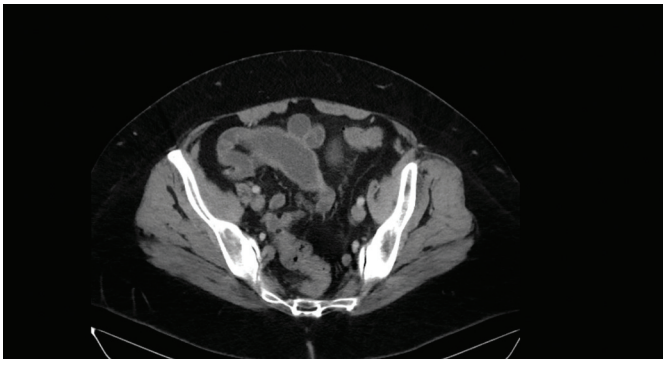

Figure 1. Transverse Abdominal Computed Tomography demonstrating isolated small bowel stricture.

The patient was then given a "dummy" capsule in preparation for possible formal capsule endoscopy approximately one week after discharge. Serial abdominal x-rays demonstrated failure of the capsule to traverse the small bowel into the colon and eventual dissolution. The patient became intolerant of liquids and solids, and oral intake triggered crampy abdominal pain. The patient was subsequently admitted to the hospital with increasing abdominal pain, multiple episodes of emesis, and per os (PO) intolerance since ingesting the "dummy" capsule. CT scan confirmed the recurrent partial SBO.

During admission, the patient underwent laparoscopic hand-assisted segmental small bowel resection (12 cm ileus) with side-to-side stapled functional entero-enterostomy. During the surgery, a single stricture was identified in the jejunal portion of the small bowel. No other strictures were identified throughout the small bowel.

Surgical specimens were taken during the procedure. The specimen grossly demonstrated that the serosal surface showed congested blood vessels over the affected portion of bowel. Once the specimen was opened, the mucosa showed a 1.5 cm × 10.5 cm area of superficial ulceration. The lumen was diminished (00.3 cm in average diameter) and the intestinal wall was indurated. The healthy bowel diameter was found to be 30.5 cm in diameter. The histopathology showed evidence of ulceration and active inflammation; the margins were histologically viable.

The patient recovered well postoperatively. She has resolved her primary persistent symptoms of crampy abdominal pain, weight loss, and PO intolerance.

DISCUSSION

A COVID-19-induced hyperinflammatory state is characterized by activation of leukocytes and endothelial cells. Leukocytes release inflammatory biomarkers and endothelial cells express tissue factor and von Willebrand factor. Some elevated inflammatory markers include, but are not limited to: erythrocyte sedimentation rate, c-reactive protein, IL-2, IL-6, IL-8, and IL-10.[5] This state of elevated inflammatory biomarkers, or cytokine storm, leads to further tissue damage and elevated coagulation biomarkers. Excessive activation of the coagulation cascade can lead to disseminated intravascular coagulation (DIC), which has been frequently associated with COVID-19 patients. DIC is characterized by overactivation of both platelets and coagulation factors, with subsequent thrombosis, which can be measured by elevated D-dimer and fibrin degradation products.[5]

The combination of these factors contributes to (arterial and/or venous) thrombosis with coinciding downstream effects. In the setting of gastrointestinal vasculature, acute thrombosis does not allow sufficient time for collateral circulation to develop, thus causing ischemia and infarction of gastric tissue. When there is limited blood flow to the gastric tissue, there are diminishing opportunities to supply essential micronutrients to, and remove harmful metabolic waste from, the resident cells. The build-up of metabolic waste leads to chronic transmural inflammation and subsequent morphologic alterations. The damaged gastric tissue is eventually replaced with scar tissue in the form of submucosal and subserosal fibrosis, thus forming a stricture.[6,7] Unlike healthy gastric tissue that is adaptable and can undergo peristalsis, the fibrotic bowel does not permit seamless passage of intraluminal contents.[7] In another scenario, the damaged tissue can form ulcerations, which have the potential to perforate and form intra-intestinal fistulas with nearby bowel.[8] Both of these pathophysiologic mechanisms ultimately have the potential to lead to bowel obstruction.

In a study by Kariyawasam et al., GI manifestations are reported in 110.4–610.1% of individuals with COVID-19 at variable times of onset with variable severity.[9] These reported symptoms are generally mild and self-limited such as diarrhea, nausea, and vomiting. However, a much smaller proportion of patients present with severe GI manifestations, such as acute pancreatitis, acute appendicitis, and SBO. Immunohistochemical analysis of our patient's small bowel biopsy showed inflammation, which is similar to other well documented extrapulmonary manifestations of COVID-19. Furthermore, gross examination of our patient's damaged bowel showed occluded vessels, which further supports the formation of microthrombi and subsequent bowel obstruction secondary to COVID-19.

The literature documents various cases extrapulmonary manifestations of COVID-19 secondary to a hyperinflammatory state. In the cardiovascular system, immunohistochemical analysis of endomyocardial biopsy demonstrate inflammation with increased lymphocytes. These findings have been isolated in cases presenting with myocarditis, arrhythmias, and autonomic dysfunction.[10] In the endocrine system, inflammatory and immunologic damage contributed to cases of Hashimoto Thyroiditis weeks after resolution of COVID-19 symptoms.[10]

In the neuropsychiatric system, microvascular thrombi and systemic inflammation have been hypothesized as possible mechanisms contributing to neuropathology in COVID-19.[10]

The authors feel that the most likely cause of this patient's small bowel ischemia was COVID-19. Her differential diagnosis included inflammatory bowel disease, microvascular disease, and thrombotic disease. However, based on her clinical presentation, workup and pathologic findings, COVID-19 is the most likely etiology.

CONCLUSIONS

COVID-19 can be responsible for both acute and chronic embolic and thrombotic events, potentially affecting the mesenteric vasculature. Surgeons need to maintain a high index of suspicion in patients with a history of COVID-19 for bowel ischemia, infarction, and obstruction.

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