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Case Report

Coronavirus disease 2019 (COVID-19) and ischemic colitis: An under-recognized complication

Kok Hoe Chan, MD a,⁎, Su Lin Lim, MD a, Ahmad Damati, MD a, Siva Prasad Maruboyina, MD b, Leena Bondili, MD c, Amany Abu Hanoud, MD d, Jihad Slim, MD a,d

a Department of Medical Education, Saint Michael’s Medical Centre, New York Medical College, NJ, United States
b Department of Gastroenterology, Saint Michael’s Medical Centre, New York Medical College, NJ, United States
c Department of Hematology/Oncology, Saint Joseph University Hospital, Patterson, United States
d Department of Infectious Disease, Saint Michael’s Medical Centre, New York Medical College, NJ, United States

A B S T R A C T

COVID-19 has spread worldwide, with more than 2.5 million cases and over 80,000 deaths reported by the end of April 2020. In addition to pulmonary symptoms, gastrointestinal symptoms have been increasingly recognized as part of the disease spectrum. COVID-19-associated coagulopathy has recently emerged as a major component of the disease, leading to high morbidity and mortality. Ischemic colitis has been reported to be associated with a hypercoagulable state. To our knowledge, there have not been any case reports of COVID-19 associated with ischemic colitis. Herein, we present the first case of a probable association of COVID-19 with ischemic colitis in a patient with a hypercoagulable state.

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1. Introduction

The first case of COVID-19 was caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which was reported in Wuhan, China, in December 2019 [1]. Since then, COVID-19 has spread across the globe, with more than 2.5 million individuals affected by the end of April 2020 [2]. SARS-CoV-2 has been identified as a novel enveloped RNA beta-coronavirus that belongs to the same family as SARS-CoV. Similar to those with SARS-CoV, patients with SARS-CoV-2 infection tend to present with upper and lower respiratory tract symptoms [3], as well as gastrointestinal symptoms, which can be present in up to 50% as reported by some studies [4]. Coagulopathy with elevated levels of D-dimer and fibrinogen has also been well described in COVID-19 patients and has been associated with increased morbidity and mortality [5]. Ischemic colitis, a condition that results from a lack of arterial blood supply to the colon, has been linked to hypercoagulable states [6]. To the best of our knowledge, there has been no case report of ischemic colitis described in patients with COVID-19. We are the first to report this important finding.

2. Case report

A 73-year-old gentleman with a past medical history of hypertension and end-stage renal disease on hemodialysis presented to the Emergency Department with a syncopal episode. He also complained of fever, nonproductive cough, shortness of breath on exertion and 5 to 6 episodes of bloody diarrhea for the past three days. He denied any recent use of nonsteroidal anti-inflammatory drugs (NSAIDs), antplatelets or anticoagulants. At initial presentation, he was afebrile and hemodynamically stable, and his oxygen saturation was 97% at rest in room air, while on exertion, the oxygen saturation dropped to 88%. Physical examination was only remarkable for tenderness over the left lower quadrant region, but otherwise, there was a nondistended abdomen, no guarding and no rebound tenderness. Digital rectal examination showed internal hemorrhoids and yellow tinged stool. Twelve hours postadmission, he complained of sudden, severe left lower quadrant cramping pain with bright red blood from the rectum. Vital signs were stable throughout admission with no episodes of hypotension. His hemoglobin was low, at a level of 5.6 g/dL (13.5–17.5 g/dL), and the mean corpuscular volume (MCV) was 86.1 fL (81.2–95.1 fL), iron was 18 μg/dL (50–150 μg/dL), TIBC was 98 μg/dL (250–400 μg/dL), and iron saturation was 18.4% (20–55%). White cell counts showed leukopenia 3.8 (4.4–11 × 10⁹/μL), lymphopenia with an absolute lymphocyte count of 600 (900–2900/μL), and the lactic acid level was 2
(0–2 mmol/L). Chest X-ray showed diffuse bilateral reticular infiltration with ill-defined areas of opacity (Fig. 1). Computed tomography (CT) of the abdomen and pelvis showed mucosal hyperenhancement with mass-like thickening of the distal sigmoid colon, and regional air within the mesenteric vessels as a concern for ischemic colitis was also noted (Fig. 2). CT of the chest noted cardiomegaly, small bilateral pleural effusions and a focus of rounded ground-glass opacities in the anterior right upper lobe (Fig. 3). Lactate dehydrogenase (LDH) was normal at 158 U/L (122–222 U/L), and other inflammatory markers were all significantly elevated: D-dimer was 4226.0 ng/mL (0–500 ng/mL), ferritin was 783 ng/mL (24–336 ng/mL), C-reactive protein (CRP) was 7.7 mg/dL (0–0.8 mg/dL), and procalcitonin was 1.65 ng/ml (0–0.5 ng/mL). A nasopharyngeal swab for SARS-CoV-2 RT-PCR was positive. The prothrombin time was 13.5 s (9.9–13 s), and the INR was 1.18 (0.9–1.1).

Sigmoidoscopy or colonoscopy was not performed, as the patient presented with typical symptoms of ischemic colitis with sudden left lower quadrant cramping pain with bloody diarrhea, and CT findings demonstrated mucosal hyperenhancement with mass-like thickening of the distal sigmoid colon and regional air within the mesenteric vessels. The patient was initially managed conservatively with bowel rest and intravenous fluids, and the antibiotics ciprofloxacin and metronidazole were started. Surgery was considered, and the surgical team did not feel that a surgical intervention would be of benefit. Anticoagulation was also started in light of the hypercoagulable state but was put on hold after a significant drop in hemoglobin was observed. On day 5 of admission, he had cardiac arrest, and the ACLS protocol was initiated for 20 min with no return of spontaneous circulation. He expired on day 5 of admission. On the day of expiration, all inflammatory markers were significantly elevated: LDH of 275 U/L, D-dimer of 3239 ng/mL, ferritin of 1713.5 ng/mL and CRP of 14.2 mg/dL.

3. Discussion

COVID-19 is a public health emergency. The World Health Organization (WHO) designated the disease as coronavirus disease 2019 in February 2020 and subsequently declared it as a pandemic in March 2020 after worldwide spread [7]. COVID-19 has multifaceted presentations, with symptoms ranging from asymptomatic to rapid multiple organ dysfunction syndrome, and has high mortality. A critical disease presentation with shock, acute respiratory failure and multiorgan dysfunction has only been reported in approximately 5% of cases, with an overall case fatality rate of 2.3% [8].

In addition to pulmonary symptoms that are typically described in patients with COVID-19, gastrointestinal symptoms such as abdominal pain, nausea, vomiting, non-bloody diarrhea and transaminitis have been identified as part of the disease spectrum [9-11]. Some case series have noted that 3% to 10% of COVID-19 patients initially present with isolated gastrointestinal symptoms [11]. It has been well recognized that the target viral receptor for this novel beta-coronavirus is the angiotensin-converting enzyme 2 (ACE-2) receptor [12-14]. ACE-2 is
not only expressed in alveolar cells but also highly expressed in the esophagus, gastric epithelial cells and small intestinal as well as colonic cells [13-16]. Moreover, SARS-CoV-2 RNA has been found in fecal samples from patients with COVID-19 [12], indicating the potential for this virus to invade the gastrointestinal tract.

Ischemic colitis is a condition resulting from a decreased blood supply to the colon leading to mucosal injury, cellular ischemia and necrosis [17]. Multiple etiologies of ischemic colitis have been described, and they are divided into occlusive (acute embolic and thrombotic occlusion, mesenteric vein thrombosis and venous thrombosis) and nonocclusive (hypoperfusion secondary to hemydialysis, shock, pancreatitis and cardiac failure) [18]. The clinical presentation of ischemic colitis can be divided into three stages. Patients will initially present with severe abdominal pain with bloody diarrhea and hyperactive bowel sounds, followed by the paralytic phase with diffuse abdominal pain and the absence of bowel sounds; the last phase is known as the shock phase, which is characterized by metabolic acidosis [19,20]. The “watershed” areas of the colon (rectosigmoid junction and splenic flexure) are particularly prone to ischemia with limited collateral blood circulation [21]. Thrombosis forming around this area will lead to colonic ischemia or ischemic colitis.

Hypercoagulable states have been recognized as one of the risk factors for ischemic colitis, although the extent of how the coagulable state leads to ischemic colitis is not well understood. COVID-19-associated coagulopathy is a well-defined phenomenon and has been associated with poor prognosis [22]. COVID-19 patients have been reported to have marked increases in D-dimer and fibrinogen levels, which predispose them to a high risk of micro- and macro-circulatory thrombosis [22]. It was suggested that the hypercoagulability observed in COVID-19 was related to the high inflammatory state associated with a “cytokine storm” rather than a progression of disseminated intravascular coagulation (DIC) [23]. To the best of our knowledge, SARS-CoV-2-induced ischemic colitis has never been reported in the literature.

Our patient had underlying risk factors for ischemic colitis – atherosclerotic heart disease and end-stage renal disease on hemodialysis. The observed ischemic colitis in the setting of COVID-19 infection with elevated D-dimer levels is very unlikely to be merely coincidental. Moreover, our patient was hemodynamically stable throughout his hospital stay and tolerated his hemodialysis sessions well, without hypotension, which precluded the possibility of transient or persistent hypotension that could have led to hypoperfusion and ischemic colitis. Our patient’s onset of ischemic colitis was consistent with the time frame of hyperinflammatory and cytokine storms associated with his viral illness. He presented on day 5 of illness with markedly elevated inflammatory markers, specifically with high D-dimer levels. It is difficult to prove causation in this setting, but the fact that his ischemic colitis occurred during the second week of his infection with SARS-CoV-2, when his inflammatory and hypercoagulable state were evident, makes this association very likely to be related.

Treatment for ischemic colitis mainly involves supportive care with bowel rest and close observation if there is no evidence of perforation, necrosis, or gangrene [17]. Surgical intervention with colonic resection is indicated if imaging shows colon infarction and necrosis or for patients with right-sided colon involvement [24,25]. Anticoagulation is rarely indicated; nonetheless, in our patient, we started therapeutic anticoagulation in light of the high D-dimer levels and the hypercoagulable state. Anticoagulation was put on hold due to a significant drop in hemoglobin.

4. Conclusion

To our knowledge, this is the first report of SARS-CoV-2 infection causing ischemic colitis with high D-dimer levels and inflammatory markers, together with clinical and radiographical findings of ischemic colitis. This case will add to the limited literature available highlighting the possible hypercoagulable state leading to gastrointestinal complications in patients with SARS-CoV-2 infection. Bloody diarrhea and ischemic colitis may be the primary presentation in this subgroup of patients, and in light of this, prompt treatment with anticoagulation is needed to reduce morbidity and mortality.

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Declaration of competing interest

All authors declare no competing conflict of interest.

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Statement of ethics

The patient provided both verbal and written informed consent to publish the case, including the publication of images.

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