CASE REPORT

Mesenteric Ischemia: A Case of Extrapulmonary Presentation in COVID-19

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Summary

Coronavirus 2019 (COVID-19) is a predominantly respiratory infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It creates a hypercoagulable milieu, manifesting at varied extrapulmonary sites as pulmonary embolism, deep venous thrombosis, stroke, myocardial infarction, and mesenteric ischemia. The pathophysiology behind this hypercoagulability is still not entirely understood, although a heightened systemic inflammatory response to the virus is deemed responsible. We herein report a case of a 36-year-old healthy male who presented with an acute abdomen and was found to have extensive mesenteric and portal venous thrombosis with bowel gangrene. The patient underwent emergency exploration with ileal resection and end-ileostomy. The hypercoagulability panel was negative, but a postoperative chest radiograph revealed suspicious ground-glass opacities. Given the ongoing global COVID-19 pandemic, we considered testing for SARS-CoV-2. A positive test for SARS-CoV-2 led us to attribute the thrombotic event to COVID-19. With anticoagulation and supportive therapy, the patient went on to make a steady recovery. A non-specific clinical manifestation of COVID-19 necessitates considering mesenteric venous thrombosis as a differential diagnosis in patients with acute abdomen.

Keywords: COVID-19, mesenteric vein thrombosis, portal vein thrombosis, hypercoagulability

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Introduction

A pneumonia outbreak started in Wuhan, China, in December 2019, and since its inception, it has caused an enormous burden on the global economy and health infrastructure. With several variants of the virus being discovered, the most consistent manifestations include fever, respiratory, and constitutional symptoms. A range of gastrointestinal manifestations (nausea, vomiting, diarrhea, abdominal pain, pancreatitis, liver injury, and mesenteric ischemia) have been reported in 2% to 79.1% of COVID-19 patients (1, 2).

Coagulopathy has emerged as an atypical presentation with deleterious complications. Pulmonary embolism is by far the most frequently cited coagulopathy of COVID-19 (3). Albeit rare, mesenteric venous thrombosis (MVT) is a critical entity that can rapidly lead to life-threatening intestinal infarction. A state of impaired venous return with thrombosis of the vena recta or major veins secondary to a local hypercoagulable state ensues, leading to intestinal infarction (4). Although the exact incidence of MVT in COVID-19 is uncertain, some single-institution cohort

studies report an incidence of 3.8% to 4% (5, 6). The overall mortality rate in patients with COVID-19-induced mesenteric ischemia was reported to be 40% (1). Clinician awareness is thus warranted for this rare entity to achieve timely diagnosis with improved outcomes. We herein report a curious case, wherein the strong thrombogenic tendency of COVID-19 led to critical mesenteric and portal venous thrombosis.

Case presentation

A 36-year-old male presented to the emergency department with insidious, progressive, and diffuse abdominal pain for 10 days, with recent worsening and distension. He had recurring bilious vomiting and absolute constipation for 4 days and an episode of melena. He gave no history of fever, upper respiratory illness, hematemesis, or drug intake. He had an unremarkable past medical and surgical history.

On examination, he was clinically dehydrated and diaphoretic. He was afebrile with a pulse rate of 104 bpm, blood pressure of 94/60 mmHg, and a respiratory rate of 18/min, and his room air oxygen saturation was 98%. The abdomen was distended and diffusely tender with rigidity. Bowel sounds were absent, and there was a dull note on percussion all over. Digital rectal examination revealed no melena. The cardiopulmonary system revealed sinus tachycardia and normal breath sounds.

The baseline blood examination showed a normal leukocyte and thrombocyte count. The patient had non-oliguric acute kidney injury with an elevated creatinine of 4.50 mg/dL (reference range, 0.7–1.2 mg/dL). The liver function test was normal. Additionally, C-reactive protein was >350 mg/L (reference range, 0–5 mg/L), lactate was 15.0 mg/dL (reference range, 5–14 mg/dL), and the international normalized ratio was 1.33. Blood was also drawn to rule out primary hypercoagulability.

Ultrasound examination revealed dilated small bowel loops with sluggish peristalsis and ascitic fluid with thick internal septations and echoes. The contrast-enhanced computed tomography scan confirmed a high-grade ileal obstruction with bowel wall ischemia and peritonitis. The main portal vein (Figure 1), from its confluence up to the porta, appeared mildly attenuated with multiple filling defects within. The superior mesenteric vein (Figure 2) and the splenic vein showed luminal thrombosis as well. The hepatic and splenic parenchyma was normal; the sections of lung parenchyma seen on the abdominal computed tomography were also normal.

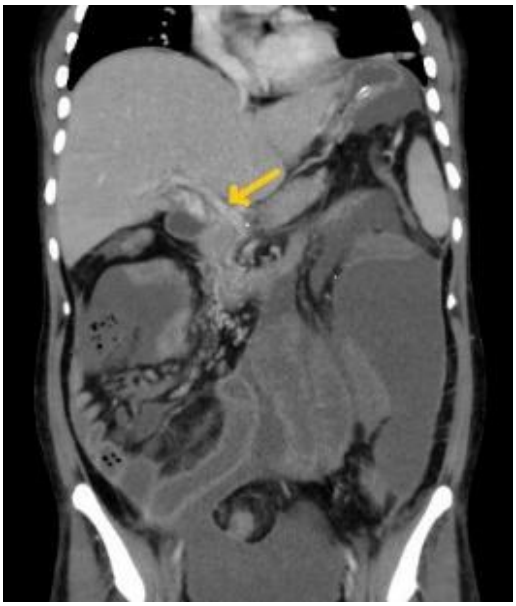

Figure 1 : Portal vein showing filling defects of luminal thrombosis (yellow arrow).

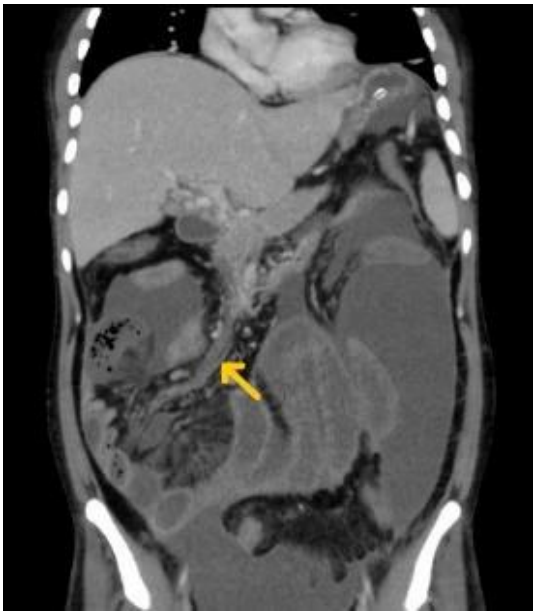

Figure 2 : Thrombosed Superior mesenteric vein (yellow arrow).

The patient was admitted to the intensive care unit. The resuscitative measures primarily focused on sepsis control. The patient responded to intravenous crystalloids and maintained a urinary output of just over 1.5 mL/kg/hour. Piperacillin-tazobactam injection was initiated empirically. Within 4 hours of admission, the patient was taken up for an emergency exploratory laparotomy, during which extensive fecal contamination within the abdomen was noted, secondary to multiple perforations within the proximal and mid-ileal ischemic segments (Figure 3). He underwent resection of approximately 150 cm of proximal and mid-ileum with a proximal end-ileostomy. The rest of the bowel and mesentery were healthy.

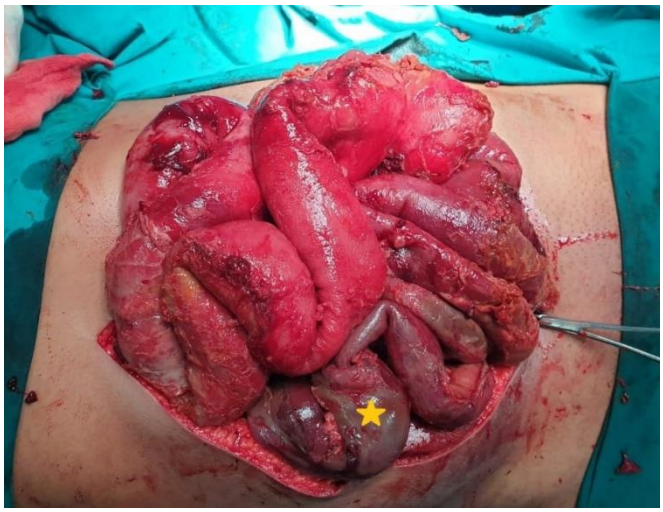

Figure 3 : Ischemic small bowel (star mark).

Tests for lupus anticoagulant, antiphospholipid antibodies, and serum homocysteine were negative. However, protein C, protein S, antithrombin III, and factor V Leiden were inconclusive, likely secondary to the pre-existing thrombotic event. The patient was started on 5000 IU of unfractionated heparin subcutaneously every 8 hours.

Chest radiographs repeated on the first postoperative day showed suspicious left lower zone opacity. Given his young age, insignificant history for MVT, and the ongoing first wave of the global pandemic of COVID-19, we sent for a nasopharyngeal swab for reverse transcription–polymerase chain reaction (RT-PCR) for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). He tested positive for COVID-19, prompting us to attribute this thrombotic event to the viral infection.

He did not suffer any respiratory manifestations secondary to COVID-19. The patient made an unremarkable, steady recovery in institutional isolation based on the current government guidelines. During his post-operative course, he developed a small burst abdomen (4×2 cm, infraumbilical) and a Southampton grade IIIb surgical site infection, which were managed with daily wound dressings until he was discharged from the hospital on the 38th postoperative day.

The patient was compliant with oral warfarin as an anticoagulant and underwent ileostomy reversal after 6 months. He continued anticoagulation for a total of 9 months and underwent a repeat thrombotic workup after discontinuing oral anticoagulation for 1 month, which yielded a negative result. We were thus able to attribute our patients' mesenteric and portal venous thrombosis to infection with SARS-CoV-2. At 11 months' follow-up, the patient is healthy, is off all medications, and has had no further thrombotic events.

Informed consent was acquired from the patient for publication of the case report.

Discussion

MVT is a relatively unusual condition, accounting for 5–15% of cases of acute mesenteric ischemia (4). MVT (60–75%) is identified in prothrombotic conditions such as heparin-induced thrombocytopenia, polycythemia vera, and essential thrombocythemia (4). Its etiology can be divided into local abdominal factors (pancreatitis, omphalitis, myeloproliferative disorders, liver cirrhosis, hepatocellular carcinoma, etc.) or inherited primary hypercoagulability (protein C, protein S, antithrombin III, and factor V Leiden deficiency) (7). MVT poses a diagnostic challenge due to its non-specific, slowly evolving presentation of critical bowel ischemia, unlike the dramatic and catastrophic presentation in mesenteric arterial thrombosis and embolism. Our case is an example of the uncommon extrapulmonary manifestation associated with the coagulopathy of COVID-19.

Few reports of similar cases have been published to date (Table 1). Among these, a consistent presentation is that of abdominal pain, with two patients having only isolated gastrointestinal symptoms, following which they tested positive for COVID-19 (8, 9).

Table 1. Summary of various cases of mesenteric and portal venous thrombosis in COVID-19

Authors	Age/sex	Time from covid-19 to presentation ofvenous thrombosis	Imaging	Anticoagulation	Treatment	Outcome
Alemán and Cevallos (14)	44/male	Positive 7 days before presenting with abdominopelvicpain	Doppler ultrasound: portal veinthrombosis CT abdomen: hypodensities and filling defects in the portal andmesenteric veins	Low-molecular-weight heparin	Conservative Discharged onwarfarin	Survived
Amaravathiet al. (9)	45/male	Diagnosed afterpresenting withfever, sore throat, epigastric pain, vomiting	CT angiography: thrombus inSMA and SMV HRCT chest: ground-glass opacity, CO-RADS grade 5	Unfractionated heparin	SMA thrombectomyand bowel resection	NR
De Barry etal. (10)	79/female	RT-PCR negative Presented with fever, epigastricpain	CT chest: ground-glass opacityand consolidation typical of COVID-19 CT abdomen: portal vein, SMV,SMA, and jejunal artery thrombosis	NR	SMA thrombectomyand bowel resection	Died
Ignat et al.(8)	28/female	Diagnosed after presenting with abdominal pain, vomiting	CT abdomen: SMV and portalvein thrombosis; small bowel ischemia	NR	Bowel resection	Survived

COVID-19, coronavirus disease 2019; M, male; F, female; CT, computed tomography; HRCT, high-resolution computed tomography; RT-PCR, reverse transcription-polymerase chain reaction; SMV, superior mesenteric vein; SMA, superior mesenteric artery; NR, not reported.

Interestingly, one patient, despite having severe pulmonary disease and extensive vascular thrombosis, tested negative for SARS-CoV-2 RT-PCR (10). Similar cases have been reported in the literature and do not invalidate the diagnosis (11).

Coagulation abnormalities associated with COVID-19 are now well known. They lead to a severe systemic inflammatory response with dysregulated complement activation and endothelial cell damage, resulting in inflammatory thrombosis. All three components of Virchow's triad have been implicated as having a putative role in the pathogenesis (12). SARS-CoV-2 is said to have endothelial cell tropism due to the expression of angiotensin-converting enzyme 2 receptor (12, 13). The direct invasion of the endothelial cells leads to the release of cytokines such as interleukin 6 and complement activation, in turn aggravating endotheliitis, with activation of monocytes and neutrophils, creating a prothrombotic state (13). Elevated factor VIII, von Willebrand factor, D-dimer, fibrinogen, and prothrombotic microparticles contribute to hypercoagulability (12, 14).

Elevated D-dimer levels in COVID-19 have been linked to a poorer prognosis with increased mortality (3, 12). Other blood parameters with variable prognostic significanceinclude elevated C-reactive protein, ferritin, lactate dehydrogenase, elevated neutrophil-to-lymphocyte ratio, and thrombocytopenia (3, 9, 15).

Three patients, including our case, had elevated C-reactive protein (10, 14). However, one of them was able to recover only with anticoagulation (14). On the contrary, Amaravathi et al. (9) reported their patient as having an elevated D-dimer with a normal C-reactive protein, possibly suggesting a resolving COVID-19 with ongoing thromboembolism necessitating bowel resection. COVID-19-induced hypercoagulability warrants prompt initiation of anticoagulation and supportive measures. Of concern, however, is the occurrence of coagulopathy despite thromboprophylaxis, even in patients with mild disease.

Conclusion

We are now more appreciative of the multitude of organ systems involved secondary to COVID-19. Non-specific gastrointestinal symptoms in COVID-19 could be misleading, and clinicians must be alert about isolated gastrointestinal manifestations, such as in our case, and thus lower the threshold for performing diagnostic abdominal computed tomography. Our case reinforces the importance of considering COVID-19-induced MVT as a higher-order differential diagnosis in patients with intestinal obstruction and elevated inflammatory markers. As more such cases come to light, vigilance and prompt intervention can be life-saving and rewarding.

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Author contributions

RS led in the conceptualization and writing of the first draft while SK contributed to reviewing and editing the original draft.

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