



Acute Mesenteric Ischemia as a Complication of COVID-19 Infection: A Case Report and Review of the Literature

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Abstract

Background: Coronavirus disease 2019 (COVID-19) is a major health problem worldwide. Vascular thrombosis is increasingly observed in COVID-19 patients. This complication seems to be due to coagulopathy and endothelial damage. In this paper, we report a COVID-19 patient with superior mesenteric artery thrombosis and review of 27 COVID-19 cases with acute mesenteric ischemia (AMI).

Case presentation: A 59-years old man with confirmed COVID-19 readmitted to the hospital due to abdominal pain and diarrhea two days after discharge from the emergency department. He was diagnosed with acute mesenteric ischemia by abdominal CT scan with contrast. The patient underwent emergency laparotomy and the ischemic gangrenous bowel was resected. Unfortunately, the patient succumbed one month after the operation.

Conclusion: AMI is a life-threatening thrombotic event rarely seen in COVID-19 patients, so it is vital to diagnose it. Anticoagulant and anti-inflammatory prophylactic therapies might be useful in preventing AMI, especially in the patients with thrombosis risk factor. So, it is crucial to reduce its incidence in COVID-19 patients.

Keywords: COVID-19, Hypercoagulopathy, Mesenteric ischemia, SARS virus, Thrombosis

1. Background

Coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 is a respiratory infection observed in Wuhan, China, for the first time. Although most COVID-19 patients have mild symptoms, some critically ill cases may present severe symptoms like acute respiratory distress syndrome (ARDS), acute kidney injury, hepatic failure, cardiac injury, and might require admission to an intensive care unit (ICU) (1).

Thrombosis, including pulmonary embolism, deep venous thrombosis and acute mesenteric ischemia (AMI), has been reported increasingly in the COVID-19 patients in this pandemic (2). Its pathophysiology is not precisely determined, but researchers suggested that coagulopathy due to the imbalance in coagulation homeostasis with the elevation of fibrinogen, and D-dimers might lead to venous and atrial thrombosis in severe COVID-19 patients (3).

Mesenteric ischemia is a life-threatening emergency health condition that results from inadequate blood flow in the mesenteric circulation. If left untreated, might lead to intestinal necrosis (4). Due to AMI's devastating complications and its high mortality rate, early diagnosis and appropriate treatment is vital.

Here, we report a case of COVID-19 and AMI, besides 27 similar cases are reviewed in the literature.

2. Case Report

A 59-year-old man with a history of ten days of fever, shortness of breath, infrequent recurrent abdominal pain, headache, general pain, weakness, and nausea without vomiting was referred to our hospital emergency department. The patient's past medical history included opioid addiction and alcohol usage. His medication history included carbamazepine, chlorthalidone, and tramadol. Initial examination revealed blood pressure of 140/70 mmHg, pulse rate of 100 beats/minute, O₂ saturation of 84 %, axillary temperature of 38.5 °C, and body mass index (BMI) of 33kg/m². The detail of laboratory findings are shown in Table 1.

The Chest computed tomography (CT) scan showed ground-glass opacity in both lungs that were highly suggestive for the COVID-19 infection (Figure 1). This diagnosis was confirmed by real-time polymerase chain reaction (RT-PCR). Six days after hospitalization, clinical manifestations improved, and O₂ saturation rose to 92%. Then, the patient was discharged with ciprofloxacin, aspirin, and famotidine. Two days later, the patient readmitted to the hospital with progressive, intermittent lower abdominal pain, watery diarrhea, and anorexia. The laboratory tests are summarized in Table 1. An abdominal x-ray and an abdominal CT scan with IV contrast demonstrated multiple air-fluid levels in the small bowel and

Table 1. Laboratory values

Measure	First Admission	Second Admission
WBC (/μL)	4700	3800
Neutrophils%	30	80
Platelet (/μL)	140000	-
Ferritin (ug/L)	1650	1230
CPK (U/L)	367	633
LDH (U/L)	-	1213
PH	7.3	7.24
pCO2 (mmHg)	54.8	29
HCO3 (mEq/L)	26	23
ESR (mm/hr)	50	15
CRP (mg/L)	146	133

WBC: white blood cell; CPK: creatine phosphokinase; LDH: lactate dehydrogenase; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein

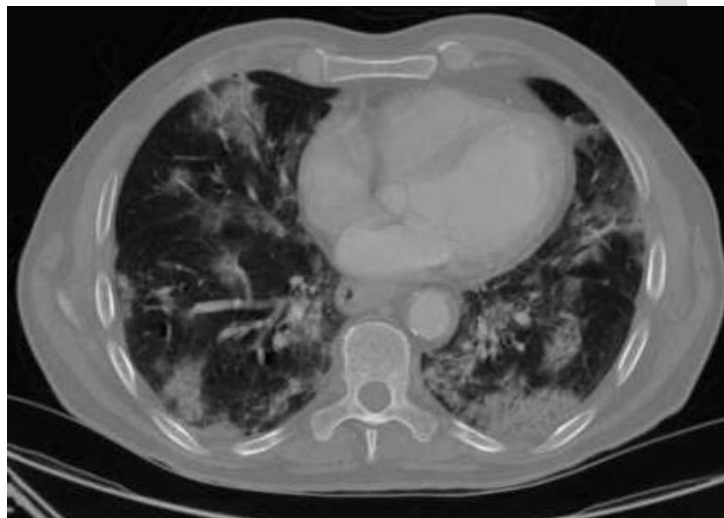


Figure 1. The Chest computed tomography (CT) scan showed ground-glass opacity in both lungs, highly suggestive for COVID-19 pneumonia

complete obstruction of the superior mesenteric artery (SMA) with a calcified plaque at its origin (Figure 2 and 3).

So, the intravenous heparin infusion was prescribed and the patient prepared for emergency laparotomy. During the operation, the pulseless SMA with small bowel gangrene in the terminal ileum and ischemia of the entire jejunum and colon was reported. Aortomesenteric bypass between SMA and the left common iliac artery, and resection of the gangrenous bowel was performed. The two ends of the intestine were closed temporarily. After 24 hours, a second-look operation was performed. Vascular grafts and the rest of the intestines had adequate blood flow, so side to side ileocolic anastomosis was made.

Fourteen days later, the patient readmitted with an anastomosis leak and enterocutaneous fistula without clinical sepsis. According to extensive pneumonia by COVID-19 (90% of both lungs) and superinfected with severe ventilator-associated pneumonia (VAP), unfortunately, the patient expired one month after surgery.



Figure 2. An abdominal x-ray shows multiple air-fluid levels in the small bowel

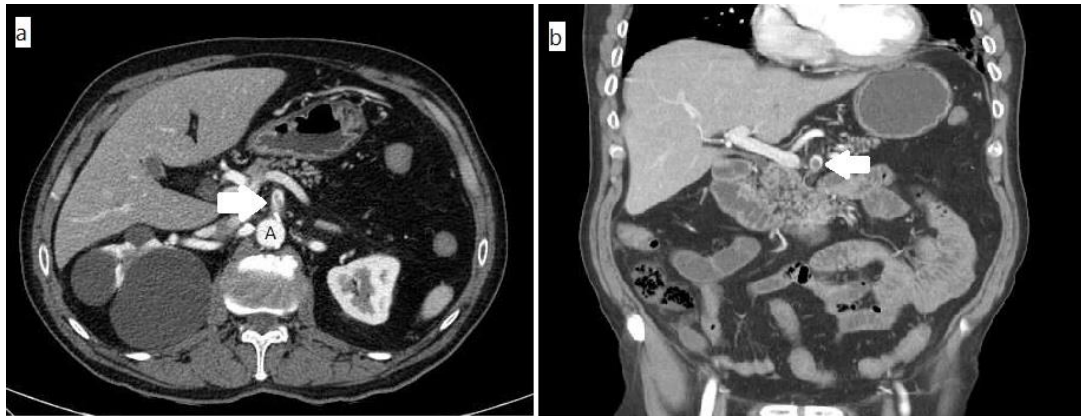


Figure 3. Abdominal CT scan with IV contrast. Axial (a) and coronal (b) section, white arrow revealed the complete thrombosis of SMA with the calcification at its origin. (A; aorta), SMA; superior mesenteric artery

3. Discussion

Acute mesenteric ischemia is a life-threatening health condition caused by a lack of blood flow in the mesenteric circulation. The mortality rate of AMI is reported at 5.3 per million each year (5). Moreover, post-surgical mortality rate without revascularization is about 80% (6). In this paper, we reported a 59 years old man with a ten-day history of COVID-19 infection. He had some atherosclerotic risk factors likewise smoking, alcohol consumption, and obesity. An abdominal CT scan with IV contrast demonstrated completed obstruction of the superior mesenteric artery (SMA). Although SMA and celiac trunk had calcified plaque at the location of branching from the aorta, it seems that the most important cause of complete occlusion of these two arteries was the hypercoagulopathy status caused by COVID-19 disease and its increased inflammation state in this patient.

We performed a literature review of PubMed, Scopus, Web of Science, and google scholar databases

to retrieve COVID-19 associated AMI case reports and evaluate demographics, clinical presentations, and outcomes. We used keywords: "COVID-19", "SARS-CoV-2", "mesenteric", "intestinal", "bowel", "ischemia", and "thrombosis" for finding English language articles.

Our database search retrieved 27 reported COVID-19-AMI cases with a mean age of 57.4 (82 - 9) years old (7 - 26). The mean timing of AMI diagnosis was 8.1 days after admission. The clinical and laboratory characteristics of all cases are presented in Table 2. Twenty patients were male, and six were female, and the gender of one patient was not reported. The most common initial clinical presentations were fever (48%) and cough (48%) followed by abdominal pain (33%). Vomiting (22%), shortness of breath (18%), and diarrhea (7.4%) were other clinical features of these patients.

The most frequent comorbidities were diabetes mellitus (24%) and hypertension (23%). However, 23% of cases had no comorbidities. Eventually, ten patients were expired, while two cases passed away

Table 2. Clinical features and laboratory findings of 27 previously reported cases of Covid-19 with acute mesenteric ischemia.

Author	N	Age	Sex	Clinical presentation	Timing of AMI diagnosis	WBC ($\times 10^9$ /L)	PLT ($\times 10^3$ / μ L)	D-dimer (mg/L)	CRP (mg/L)	Treatment of AMI	Outcome
Vartanoglu Aktokmakyan et al. (7)	5	Mean 61.2	5 Male	4 Cough, 3 Fever, 3 Dyspnea	NR	Mean 8.67	Mean 230 (73-359)	Mean 0.447 (0.321-675)	Mean 970 (200-1820)	NR	4 Discharged, 1 Died
Ignat et al. (8)	3	Mean 50.3	2 Male, 1 Female	2 ARDS, 1 Abdominal Pain, 1 Vomiting,	Mean Day 6.6	NR	NR	NR	NR	2 Small Bowel Laparotomy and Resection, 1 Conservative Management	1 Died, 1 Discharged, 1 Still in Hospital
Al Mahruqi et al. (9)	2	Both 51	1 Male, 1 NR	1 Shortness of Breath, 1 Fever, 1 Abdominal Pain, 1 Poor Oral Intake	Day 13	30,16	NR	2.5,10	NR	Both Laparotomy, 1 UFH	1 Discharged, 1 Died
Sehhat etl al. (10)	1	77	Male	Shortness of Breath	Day 11	4.1	146	NR	86	Laparotomy	Died
Azouz etl al. (11)	1	56	Male	Acute Ischemic Stroke	Day 2	NR	NR	NR	NR	Small Bowel Laparotomy and Resection	Discharged

Table 2. Continued

Cheung et al. (12)	1	55	Male	Abdominal Pain, Diarrhea, Nausea	Day 12	12.46	100	3.4 (nmol/L)	NR	Exploratory Laparotomy and SMA Thromboembolctomy, Heparin Infusion	Discharged
Azhdeh et al. (13)	1	54	Male	Cough, Shortness of Breath, Fever and Chills	NR	13.9	477	NR	+1	Small Bowel Laparotomy and Resection	Discharged
Kielty et al. (14)	1	47	Male	Fever, Cough and Vomiting	Day 10	NR	NR	NR	NR	Therapeutic Heparin	Discharged
Mitchell et al. (15)	1	69	Male	Abdominal Pain, Constipation, Eructation	Day 1	NR	NR	NR	NR	Small Bowel Resection and SMA Thromboembolctomy	Discharged
Beccara et al. (16)	1	52	Male	Fever and Cough	Day 13	NR	NR	NR	44	Intestinal Resection	Discharged
Vulliamy et al. (17)	1	75	Male	Abdominal Pain, Vomiting, Cough	Day 1	18.1	497	23.6	NR	Small Bowel Laparotomy and Resection	NR
Barry et al. (18)	1	79	Female	Fever, Abdominal Pain	Day 1	12.6	NR	NR	125	SMA Thromboembolctomy and Laparotomy, Resection of Necrotic Ileum and Right Colon	Died
Khesrani et al. (19)	1	9	Female	Fever, Abdominal Pain, Vomiting, Diarrhea	NR	1.14	4	NR	240	Resection of the Ischemic Bowel Loop With Double Ileostomy	Died
Norsa et al. (20)	1	62	Male	Abdominal Pain and Bilious Vomiting	NR	elevated	NR	elevated	elevated	Small Bowel Resection	Died
Singh et al. (21)	1	82	Female	Fever, Shortness of Breath, Cough	Day 18	22.8	146	1.3	308	Ileostomy	Discharged
English et al. (22)	1	40	Male	Severe Dyspnea, Fever and Cough	Day 10	8.6	NR	13.7	NR	Small Bowel Laparotomy and Resection	Discharged
Krothapalli et al. (23)	1	76	Female	Shortness of Breath	Day 14	9	NR	2.15	7.97	Conservative Management	Died
Soeselo et al. (24)	1	65	Male	Fever, Cough, Dyspnea	Day 7	9	222	0.78	2	Small Bowel Laparotomy and Resection	Died
Hanif et al. (25)	1	20	Female	Fever, Cough	Day 7	NR	633	2.34	620	Small Bowel Laparotomy and Resection	Discharged
Bagheripour et al. (26)	1	78	Male	Abdominal Pain, Cough, Dyspnea, Nausea, Vomiting	Day 1	11.2	146	301	Elevated	Conservative Management	Died

NR: not reported; UFH: unfractionated heparin; ARDS: Acute respiratory distress syndrome; CAD: coronary artery disease; HF: heart failure; AF: atrial fibrillation; SMA: superior mesenteric artery; WBC: white blood cell; PLT: platelet; CRP: C-reactive protein.

without any comorbidities. Treatment regimen of COVID-19 in most cases was not reported, but commonly the reported treatments regimens included azithromycin, hydroxychloroquine, dexamethasone, ceftriaxone, lopinavir, ritonavir, methylprednisolone, and enoxaparin.

Laparotomy and resection of the bowel as a common approach of mesenteric ischemia was performed in 13 cases (48%), however, in nine cases, bowel resection was not performed. Vartanoglu Aktokmakyan et al. reported that five out of six COVID-19 patients underwent emergency surgery for mesenteric ischemia (7) and ileostomy was created in of two these cases, and SMA thromboembolctomy was performed in three other cases.

In a case reported by Kielty et al. (14) therapeutic heparin was administrated and then the patient was

discharged. In nine cases (64%), out of 14 patients, leukocytosis (WBC>11000), was reported and one patient had leukopenia (WBC<4000), the same as our case in the second admission. Fourteen patients (87%) had elevated CRP (CRP>10 mg/L), and D-dimer was elevated (D-dimmer > 0.4 mcg/ml) in all reported cases. Besides, in three patients thrombocytosis (PLT > 450000) was reported, but platelet count was not reported in many of the patients.

According to a study by Sogaard et al., the presence of intra-abdominal inflammation and systemic infections were the most important risk factors for portal vein thrombosis (27), however, two cases reported by Mitchell et al. (15) and English et al. (22) had a stroke and portal vein thrombosis, respectively, but most of the patients did not suffer

from other thromboembolic events like PTE or stroke.

In the AMI, the key point is administration of life-saving treatment like revascularization (medical or surgical) before the progression of ischemia to intestinal gangrene and it depends on early diagnosis. If treatment be delayed more than six hours after the onset of mesenteric ischemia, it will be associated with a significant increased mortality rate (28).

Unfortunately, no specific criteria have already been proposed for the early diagnosis of mesenteric ischemia. Therefore, the best treatment for this disease is prevention by early diagnosis of the high risk patients. Hence, it was shown that all inflammatory markers were significantly elevated in the patients with mesenteric ischemic and COVID-19. Moreover, studies revealed that the pathogenicity of COVID-19 has been increasingly attributed to the systemic inflammatory response (SIR) leading to disseminated intravascular coagulation (3).

Yet, there is no consensus whether the coagulation disorders are a secondary response to the SIR or are developed directly by COVID-19 infection. Some studies revealed the incidence of peripheral ischemia and stroke are mediated by antiphospholipid antibodies (29). However, multiple factors seems to be responsible for development of AMI in COVID-19 patients. Foremost, COVID-19 enters the cell through the receptor of the angiotensin-converting enzyme two (ACE₂) in the alveoli and, creates a severe form of infection with SIR expression in various organs, including vascular endothelial cells (30, 31). Hence, the entrance of SARS-CoV-2 to endothelial cells, can cause cellular damage and release Von-Willebrand Factor (VWF), which results in endothelial thrombosis.

Next, the cytokine-storm that is caused by increasing the blood level of interleukins one and six and interferon-g, have been reported in these patients (32). Diabetes mellitus, hypertension and atrial fibrillation are known as the main risk factors of AMI (33, 34).

There are some signs and symptoms like abdominal distension, nausea, vomiting and diarrhea, when observed in patients with COVID-19, more evaluation like an abdominopelvic CT scan are necessary to rule out the AMI.

Consequently, it seems the use of preventive therapies for mesenteric ischemia in patients with COVID-19 is an important strategy. Prophylactic or therapeutic anticoagulation in patients with thromboembolic risk factors might be effective to reduce the incidence of such complications and improve the prognosis of AMI (35). According to the high worldwide prevalence of COVID-19 and its significant mortality, more studies about COVID-19 and AMI are recommended.

4. Conclusion

AMI is a critical health condition that its early diagnosis is crucial for life saving. Although, some studies have reported the relationship between AMI and COVID-19, but further studies are needed to understand this relationship more precisely and reach to proper approaches to prevent AMI in these patients.

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