

## Case Report



# Acute Mesenteric Ischemia in a Patient with COVID-19: A Case Report

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## Abstract

The severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) presents clinical manifestations similar to the influenza, severe acute respiratory syndrome (SARS-CoV), and Middle East respiratory syndrome (MERS-CoV). However, in the course of the coronavirus disease 2019 (COVID-19), various pathological complications of high clinical significance have remained unknown. Impaired blood supply to the visceral vascular system can cause serious life-threatening acute damage. We report a case of extensive acute mesenteric ischemia associated with SARS-CoV-2 infection confirmed in a patient hospitalized in Amin Hospital – a COVID-19 referral center in Isfahan University of Medical Sciences, Isfahan, Iran. This case highlights the importance of paying attention to serious and less common or less known clinical manifestations other than fever, dry cough, dyspnea, and myalgia.

**Keywords:** COVID-19, Mesenteric Ischemia, Pneumonia, SARS-CoV-2

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## Introduction

In December 2019, the new coronavirus disease 2019 (2019-nCoV), nowadays known as severe acute respiratory syndrome coronavirus 2 with the acronym SARS-CoV-2, originated in Wuhan city of Hubei province of China, and quickly spread around the world due to its highly contagious nature.<sup>1</sup> The SARS-CoV-2 spreads faster than its previous two predecessors, SARS-CoV and MERS-CoV, but it seems to have a lower mortality rate.<sup>2</sup> Human angiotensin-converting enzyme II (ACE2) expressed on the surface of cell membrane in different tissues act as receptors for the Spike surface glycoprotein of SARS-CoV-2, which appears to be the main portal of entry. ACE2 catalyzes the hydrolysis of angiotensin II into other angiotensin subtypes, thereby lowering blood pressure by counteracting the activity of the ACE. Inhibition of ACE2 enzyme by binding to the SARS-CoV-2 spike protein augments the concentration and effects of angiotensin II through reducing the hydrolysis of angiotensin II as well as activating the renin-angiotensin system (RAS).<sup>3</sup> ACE2 is highly expressed on the outer surface of cells in the respiratory system, intestines, kidneys and the cardiovascular system. COVID-19 infection may cause several serious disorders in these organs through a decrease in ACE2 expression, excessive activation of the renin-angiotensin system, and elevation of angiotensin II levels. The effect of COVID-19

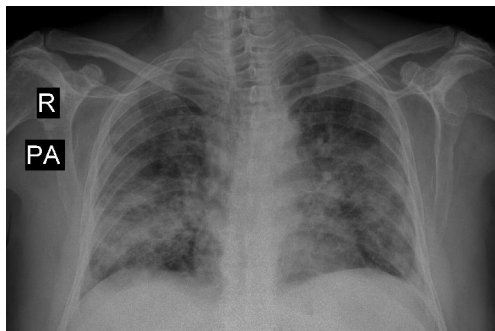
infection on suppressing ACE2 activity and promotion of RAS pathway activity in the cardiovascular and respiratory systems causes complications in susceptible patients, including hypertension, congestive heart failure, platelet aggregation, atherosclerosis, lung edema, acute respiratory failure, pulmonary embolism, and fibrosis.<sup>4</sup> Also, many of the features reported for COVID-19 are similar to SARS-CoV infection, which may lead to prolonged coagulation, lymphopenia, and D-dimer elevation.<sup>4</sup> In addition to injuries inflicted on the cardiac and respiratory system due to elevation of angiotensin II concentration, ACE2 expression deficiency in the kidneys, vascular endothelial cells and the intestinal epithelial cells indicates a possible mechanism for multiple organ disorders associated with SARS-CoV-2 infection. Thus, it is clear that the clinical features of SARS-CoV-2 disease are manifested by a wide range of clinical symptoms from asymptomatic patients to multi-organ failure.<sup>5</sup> This report presents the clinical feature of severe acute mesenteric ischemia complication in a patient with confirmed COVID-19 infection.

## Case Report

On March 17, 2020, a 77-year-old man presented to Amin hospital, a COVID-19 referral center in Isfahan University of Medical Sciences, Isfahan, Iran, with a 5-day history of cough and shortness of breath. On admission

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to the hospital's triage, the patient was given a mask and gloves. After about 10 minutes, the patient was referred to the emergency physician's office in the urgent care ward for examination and medical care. The patient had no history of travel in recent months. Given that a few days before the patient's presence in the hospital, the outbreak of the viral disease was officially confirmed by the Ministry of Health in Iran, and also considering the patient's clinical symptoms and history, the possibility of infection with COVID-19 was extremely strong. Therefore, the physician requested a specific COVID-19 test using rRT-PCR laboratory technique (real-time reverse transcription-polymerase chain reaction) on respiratory system samples obtained by oropharyngeal and nasopharyngeal swabs. Except for hypertension, the patient had no other underlying disease. The patient was fully conscious, and his complaint was limited to the initial respiratory symptoms. Clinical examination revealed an initial blood pressure of 130/90 mm Hg, body temperature of 37.5°C, heart rate of 110 beats/minute (bpm), respiratory rate of 29 breaths/minute and pulse oxygen saturation (SpO<sub>2</sub>) level of 86% while breathing in ambient air. Auscultation of the chest revealed rhonchi, wheezing and crackles; the chest x-ray radiograph (CXR) showed ground-glass opacification associated with progressive reticulation in lung bases (Figure 1). Considering the radiographic evidence and noting that the patient's SpO<sub>2</sub> was reduced to the low level of 86%, supplemental oxygen was administered through a nasal cannula at a rate of 2 liters per minute and his SpO<sub>2</sub> was reassessed. The patient did not have acute respiratory distress but complained of dyspnea and dry nonproductive cough. After hospitalization in the isolation ward, due to the clinical manifestations and concerns about severe pneumonia, vancomycin (Vancocin®) was co-administered with Meropenem (1 gram daily). However, the vancomycin dose was adjusted due to the patient's high serum creatinine levels: after a loading dose of 500 mg every 12 hours, the maintenance dose was 500 mg intravenously every 24 hours. A definite diagnosis of the presence of the virus was not confirmed yet using the rRT-PCR technique in samples taken from the patient's respiratory tract



**Figure 1.** Chest X-ray scan shows bilateral ground-glass opacities (GGOs) with reticulation in lower lobes.

on the first and second days after admission. However, taking into account the evidence related to the clinical manifestations, as well as the characteristics of the patient's chest CT images, COVID-19 infection was highly suspected. Therefore, according to the Iranian national guidelines for prevention, diagnosis and treatment of the COVID-19, the proposed medication regimen of the Iranian Scientific Committee of Coronavirus Combat and Prevention, antiviral drugs with hydroxychloroquine, was considered for treating this patient. Treatment with hydroxychloroquine (400 mg q12h as loading dose on day one, continued on the following days at 200 mg q12h) and lopinavir/ritonavir (200 mg/50 mg Kaletra®) 2 tablets every 12 hours with cardiac monitoring was initiated. Treatment with antibiotics and antivirals continued with supportive measures. Three days after sending the samples prepared using oropharyngeal and nasopharyngeal swabs to the laboratory, the patient was diagnosed with SARS-CoV-2 using the rRT-PCR technique and the test result was positive. On the second day of hospitalization (7th day of illness), the patient was referred to the intensive care unit (ICU) due to low level of oxygen saturation and tachypnea. The patient's treatment during this time was largely supportive. In cases where it was necessary to manage the patient's clinical symptoms such as fever and pain, the patient received antipyretic therapy including 1000 mg of intravenous acetaminophen every 8 hours. In the patient's isolation unit in the ICU, laboratory tests such as serum chemical analysis, complete blood count (CBC) and arterial blood gas (ABG) test were available starting on admission day 2. The results of the patient's daily laboratory tests in the hospital reflected leukopenia, moderate thrombocytopenia as well as a significant increase in multiple measured parameters including erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), lactate dehydrogenase (LDH), creatine phosphokinase (CPK) and serum creatinine (Table 1). On admission day 7 (12th day of illness), the patient's clinical condition improved and his oxygen saturation values with oxygen mask improved to 90%; but in the afternoon of admission day 11 (16th day of illness), the patient complained of intermittent abdominal pain and intolerance to the diet. The patient was then instructed to eat nothing through the mouth (NPO) and abdominal CT scan was requested for the patient. There was no sign of vascular calcification on the abdominal CT scan. Due to the high serum creatinine level, CT-scan was done without contrast (Figure 2). Antibiotic and antiviral treatment was continued for the patient as described above. The patient's echocardiography was normal and regular sinus rhythm was evident on the electrocardiogram. The electrocardiogram showed normal sinus rhythm. Within a short time, the patient suddenly experienced severe progressive abdominal pain with leukocytosis and mild metabolic acidosis (base excess = -2.6 mmol·L<sup>-1</sup>). On initial examination, generalized tenderness

Table 1. Laboratory Findings

Measure	Reference Range	Illness Day 6,		Illness Day 7,		Illness Day 9,		Illness Day 10,		Illness Day 11,		Illness Day 12,		Illness Day 13,		Illness Day 14,		Illness Day 15,	
		Admission Day 2	Admission Day 3	Admission Day 5	Admission Day 6	Admission Day 7	Admission Day 8	Admission Day 9	Admission Day 10	Admission Day 11	Admission Day 12	Admission Day 13	Admission Day 14	Admission Day 15	Admission Day 16	Admission Day 17	Admission Day 18	Admission Day 19	Admission Day 20
White cell count (/ $\mu$ L)	3800–11,000	4200	4300	4200	4200	4900	6200	6300	24400	22900									
Red cell count (/ $\mu$ L)	4.2–5.7 $\times 10^6$	4.1 $\times 10^6$	4.1 $\times 10^6$	3.8 $\times 10^6$	3.7 $\times 10^6$	3 $\times 10^6$	4.01 $\times 10^6$	4.18 $\times 10^6$	4.32 $\times 10^6$	4.37 $\times 10^6$									
Neutrophils	50%–70%	69.5%	70.9%	64.2%	72.1%	79.8%	78.6%	85%	95.9%	90.4%									
Lymphocytes	20%–40%	19.6%	22.3%	26.2%	16.8%	14.7%	12.7%	12.2%	3.5%	3.9%									
Platelet count (/ $\mu$ L)	1.5–4 $\times 10^5$	1.46 $\times 10^5$	1.32 $\times 10^5$	1.53 $\times 10^5$	2.09 $\times 10^5$	2.64 $\times 10^5$	2.34 $\times 10^5$	2.94 $\times 10^5$	3.38 $\times 10^5$	349 $\times 10^5$									
Hemoglobin (g/dL)	13.2–17.0	12.5	11.5	11.1	11	10.7	11.2	11.9	12.2	12.3									
Hematocrit (%)	39.0–50.0	38.9	—	—	33.2	32.9	34.3	35.7	36.9	38.8									
Sodium (mmol/L)	136–145	134	137	—	—	—	140	138	140	139									
Potassium (mmol/L)	3.5–5.1	4.4	4	—	—	—	3.3	3.5	3.8	5									
HCO <sub>3</sub> <sup>-</sup> (mEq/L)	22–28	—	—	—	—	—	—	—	23.5	—									
PCO <sub>2</sub> (mmHg)	35–45	—	—	—	—	—	—	—	45.3	—									
pH	7.35–7.45	—	—	—	—	—	—	—	7.33	—									
Blood urea nitrogen (mg/dL)	9–23	39	37	—	—	21	16	11	14	36									
Creatinine (mg/dL)	0.7–1.3	2.1	1.7	—	—	1.3	1	1	2.2	3.1									
Total bilirubin (mg/dL)	0.3–1.2	—	—	—	—	—	—	—	1.7	—									
Alanine aminotransferase (U/L)	10–49	—	—	—	—	—	—	—	79	—									
Aspartate aminotransferase (U/L)	≤33	—	—	—	—	—	—	—	96	—									
Alkaline phosphatase (U/L)	46–116	—	—	—	—	—	—	—	156	—									
Creatine phosphokinase (mcg/L)	24–195	621	—	—	—	—	—	—	—	—									
Lactate dehydrogenase (U/L)	120–246	644	—	—	—	—	—	—	—	—									
Prothrombin time (s)	12.2–14.6	12.4	—	—	—	—	—	—	—	—									
INR	0.9–1.1	1.18	—	—	—	—	—	—	—	—									
Creatine kinase (U/L)	62–325	621	—	—	—	—	—	—	—	—									
CRP	Up to 6	86	60	—	88	50	—	—	80	—									
ESR	0–20	35	—	—	—	—	—	—	—	—									
Blood Group	B positive	—	—	—	—	—	—	—	—	—									

ESR, Erythrocyte sedimentation rate; CRP, C-reactive protein; INR, international normalized ratio.

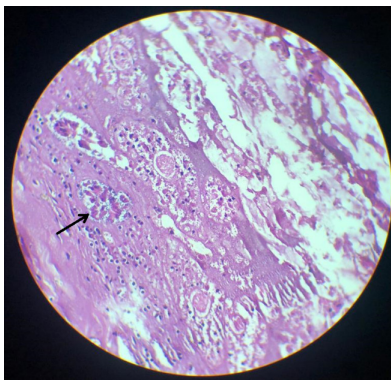
was found in the patient's abdomen. Given the abdominal CT scan and the patient's clinical presentation, a decision was made to transfer the patient to the operating room and perform laparotomy. Tissue samples were collected from the ischemic area for histopathological examination. The patient's history revealed no evidence of a hypercoagulable condition, myeloproliferative disease, venous thrombosis disorder or malignancy. However, histopathological findings revealed that small intestinal mucosa contained necrosis of the wall and hemorrhage with infiltration of inflammatory cells within full-thickness layer. In addition, on histological examination of tissue sections, extensive thrombosis was evident in mesenteric vessels. (Figure 3). Observations at laparotomy include wider ischemia more than 80 cm from the ligament of Treitz to the beginning of the hepatic flexure of the colon (Figure 4). Unfortunately, the patient died one day after surgery due to cardiorespiratory arrest.

### Discussion

Our report of acute mesenteric ischemia in a confirmed patient of COVID-19, who did not have a risk factor

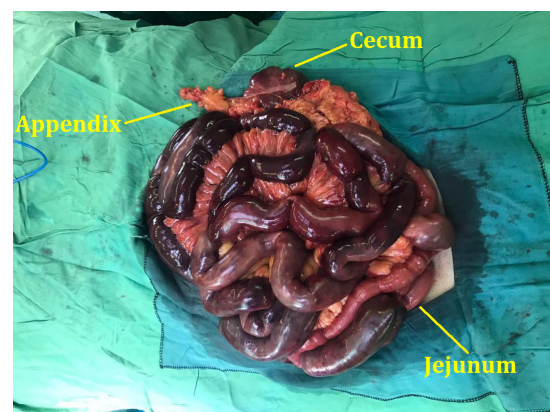


**Figure 2.** Abdominopelvic CT scan without contrast shows dilatation of the small intestine loops with wall thickening and increased thickness of the mesenteric fat.



**Figure 3.** Partial small intestinal resection with hematoxylin and eosin (H&E) stain: sections show small intestinal mucosa containing wall thickness necrosis and hemorrhage with infiltration of inflammatory cells within the full thickness layer (transmural infarction). Black arrow shows a thrombosed mesenteric vein.

for ischemic mesenteric disease, indicates various aspects of the disease that are still unknown and should be considered. In addition to affecting the respiratory tract and lungs, the disease can cause thrombogenic ischemia in various parts of the body, including the gastrointestinal tract. Currently, our clinical understanding of the entire manifestations and complications of COVID-19 is very small. Some COVID-19-related manifestations such as respiratory distress syndrome and heart disorders are among the fatal consequences of the COVID-19 disease, which have been reported mainly from China.<sup>2,5-7</sup> Initially, the patient had a mild fever, dry cough and shortness of breath that appeared on the fifth day of illness. However, 11 days after hospitalization, the patient developed severe gastrointestinal symptoms. Unfortunately, on laparoscopic examination, the extensive and thrombogenic mesenteric ischemia due to COVID-19 infection was confirmed. The patient had sinus rhythm on electrocardiography and suffered acute abdominal pain on the 11th day of hospitalization. Mesenteric ischemia is an infrequent but complicated medical condition in which injury to the small intestine occurs when narrowed or blocked arteries restrict the blood supply. The chronic form of ischemic mesentery is usually caused by the formation of atherosclerotic plaque and restriction of blood flow in the mesenteric vessels. Chronic mesenteric ischemia often has a multifactorial etiology. Diabetes mellitus, hypercholesterolemia, smoking and hypertension are the risk factors predisposing the patient to atherosclerosis associated with increased risk for chronic mesenteric ischemia. However, the most common cause of acute mesenteric ischemia (AMI) is a sudden interruption in the blood flow due to blood clots in the main artery of the mesentery. Atherosclerosis, chronic heart failure, cardiac arrhythmia, recent heart attack, valvular heart disease, and intra-abdominal malignancy are the most important risk factors for AMI. The patient had a history of hypertension, which was well controlled by medication,



**Figure 4.** Resected Segments of The Infarcted Small Intestine and Ascending Colon.

although hypertension is not a risk factor with a direct impact on the occurrence of acute ischemic mesentery. In the present study, we showed a case of AMI in a confirmed COVID-19 patient, who did not have a risk factor for ischemic mesenteric disease. Therefore, considering the possible role of the SARS-CoV-2 virus in the tendency to thrombosis, this complication can be justified.

In conclusion, although most of the reported symptoms of the coronavirus disease 2019 are related to the respiratory system, there is concern that the occurrence of serious and life-threatening manifestations such as mesenteric ischemia in the gastrointestinal tract may be overlooked.

#### Authors' Contribution

SS, SSh and AH: designed and supervised the study. SSh: wrote the manuscript draft, analyzed and interpreted the results, and assistance in the final revision. AH: data analysis and participation in the final revision. HT, HM and AR: effective participation in the preparation and documentation of evidence. ALH: study design and coordination with authors.

#### Conflict of Interest Disclosures

The authors declare that they have no conflict of interest.

#### Ethical Statement

This study was designed based on the ethical principles of the Declaration of Helsinki (2008) for medical studies involving humans.

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