Published online 2022 December 20 **Case Report**

# Extensive Bowel Necrosis in a Case of COVID-19 Disease Despite Warfarin Toxicity: A Paradoxical Event

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**Received** 2022 June 22; **Revised** 2022 July 15; **Accepted** 2022 October 06.

**Abstract**

**Background:** Coronavirus disease 2019 (COVID-19) involves multiple organs, including the gastrointestinal tract. It also causes frequent thromboembolic events because of its thrombogenicity. This study reports a COVID-19 case of extensive bowel necrosis despite using warfarin.

**Case Presentation:** A 52-year-old homeless addict male was brought via Emergency Medical Services with a chief complaint of abdominal pain for two days and loss of consciousness since the day before. He had a history of cough and dyspnea for seven days and had been using warfarin after mitral valve replacement three years earlier. On admission, he had low oxygen saturation, tachycardia, and fever. Because of his respiratory signs and symptoms, a chest CT scan was performed, and evidence of COVID-19 infection was detected. He had nausea, and on abdominal examination, there was generalized tenderness, rebound tenderness, and guarding. Following physical examination and abnormal laboratory test results, he underwent an emergent laparotomy. Extensive necrosis made surgical intervention impossible, and he died shortly after the surgery.

**Conclusion:** COVID-19-associated coagulopathy raises many challenges nowadays, and according to the present case, even using anticoagulants may not prevent it.

*Keywords:* ACE-2 receptors, Bowel necrosis, COVID-19, Vasculitis, Warfarin toxicity

## 1. Background

The coronavirus disease 2019 (COVID-19), which was first seen in China, has affected millions worldwide. It was declared a pandemic by the world health organization on March 11, 2020 (1). COVID-19 patients usually have pulmonary involvement, with fever, generalized fatigability, and dry cough being the most frequent symptoms (2).

Coronavirus or severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) binds to host cells via antigen-converting enzyme-2 (ACE-2). Although in all major organs, ACE-2 mRNA is present, initiation of the infection would depend on protein expression. In several organs, including lungs, abdomen, small intestine, nasopharynx, spleen, oropharynx, hepatic, brain, and renal, binding to these receptors occurs on epithelial, endothelial, and enterocyte cells. In addition, the density of ACE-2 receptors is high in organs such as the lungs, heart, veins, and arteries (3). As the gastrointestinal tract (GIT) also expresses ACE-2 receptors, its involvement can happen with common manifestations of diarrhea, nausea, and vomiting (4).

Frequent thromboembolic events have occurred even in those who were treated with anticoagulants due to the thrombogenicity of this infection (5). Thrombogenicity can be caused by several mechanisms, such as inflammation, activation of tissue factor pathway, endothelial injury via ACE-2 receptors, increased fibrin formation, higher thrombin generation, polymerization with fibrinolysis shutdown, and increased blood viscosity by hypoxia (6,7).

This study reports a COVID-19 case of extensive bowel necrosis despite using warfarin because of mitral valve replacement. At the time of admission, the international normalized ratio (INR) was 6.4.

## 2. Case Presentation

A 52-year-old homeless addict male was brought via Emergency Medical Services (EMS) with a chief complaint of abdominal pain for two days and loss of consciousness since the day before. The source of history was his homeless friend. He also had a cough and dyspnea for seven days and had been using warfarin after mitral valve replacement three years earlier. He had not received any COVID-19 and was treated for his symptoms before being taken to the hospital.

Because the COVID-19 infection was not confirmed for him before, no medication had been used in this case. On admission, he had an oxygen saturation of 70%, which could improve with a nasal cannula to 90%, a heart rate of 140 beats/min, a respiratory rate of 20/min, and a temperature of 38.2°C. Due to his respiratory signs and symptoms, a chest CT scan was performed in which evidence of COVID-19 infection was detected. He had nausea, and

**Table 1.** Laboratory investigations

| WBC | Platelets | Neutrophils | lymphocytes | Hb | PH | pCO2 | HCO3 | PT | PTT | INR | BUN | LDH |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 37.4 | 560,0000 | 90% | 4% | 8.6 | 7.33 | 29.5 | 15.8 | 64 | 96 | 6.4 | 261 | 1988 |

WBC: white blood cell; Hb: hemoglobin; pCO2: partial pressure of carbon dioxide; HCO3: Bicarbonate; PT: Prothrombin time; PTT: partial thromboplastin time; BUN: blood urea nitrogen; LDH: levels of lactic acid dehydrogenase.

on abdominal examination, there was generalized tenderness, rebound tenderness, and guarding.

Laboratory results showed a high INR, neutrophil dominant leukocytosis, low hemoglobin levels, metabolic acidosis, high partial thromboplastin time (PTT), prothrombin time (PT), high blood urea nitrogen (BUN), high levels of lactic acid dehydrogenase (LDH), and increased platelets (Table1).

According to the physical examination and laboratory test results, he was a candidate for emergent laparotomy. Ceftriaxone and metronidazole were prescribed for him before the surgery was performed under general anesthesia with a midline incision. From 50 cm distal to the ligament of Treitz, there were multiple yellowish necroses every 4-5 cm up to a point that was 10 cm to the ileocecal valve. Between these patches, there were ischemic parts without any perforation (Figure 1). The patient was considered inoperable because of extensive necrosis, so the abdomen was closed. The patient was transferred to the ICU while he was intubated and died shortly after the surgery.

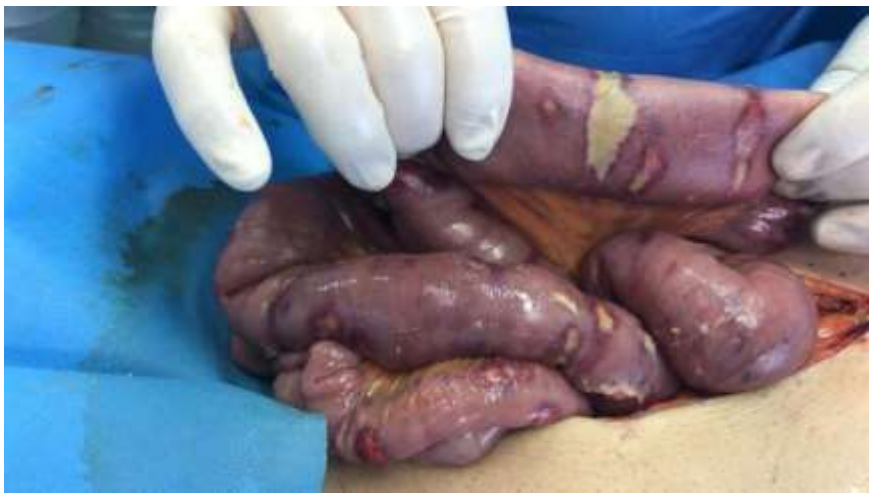

**Figure 1.** Patchy yellowish necrosis in all parts of the small intestine

## 3. Discussion

COVID-19 patients can have a chief complaint of gastrointestinal symptoms, such as abdominal pain, vomiting, and diarrhea during their disease. The high prevalence of venous thromboembolism in hospitalized non-ICU patients and critical ones requiring intensive care should make us think about thromboembolic events in all organs due to the high mortality of these events (8).

These events in the GIT can occur because of severe systemic inflammation or they can be potentially caused by binding SARS-CoV-2 to the ACE-2 receptor that results in local and viral replication, infection, and cytotoxic events (9).

Clinically, ischemic bowel disease varies from mild to severe conditions, such as bowel perforation, peritonitis, and septic shock. Radiologic findings are mostly non-specific, and the same appearance is seen in infectious and inflammatory colitis (9). Reduced blood flow would result in bowel necrosis, which can cause infection, obstruction, inflammation, and vascular occlusion. The most common cause of intestinal necrosis is acute mesenteric occlusion; however, inflammation can cause this necrosis in COVID-19 patients (10). Although the patient under study was treated with warfarin, presumably the inflammation and micro thrombosis led to bowel necrosis. Therefore, bowel necrosis can lead to death without early intervention and proper surgical treatment (9).

Generally, taking direct oral anticoagulants for atrial fibrillation cannot completely prevent thromboembolism, and anticoagulation failure of these medications is not uncommon (11). Based on a previous study, oral anticoagulant failure is observed in antiphospholipid syndrome, atrial fibrillation, and deep vein thrombosis (12). Therefore, to avoid thromboembolism recurrence in these patients, a different oral anticoagulant with an alternate mechanism of action should be considered (11).

Anticoagulant therapy in severe COVID-19 infection is a matter of argument. Prophylactic-dose heparin has

been chosen as the standard of care because of its beneficial effects in some studies early in the pandemic. Some studies showed no benefit in using heparin for critically ill patients. However, some other studies found therapeutic effects of anticoagulation in patients not yet requiring ICU support (13).

Based on the present study, bowel necrosis, regardless of anticoagulant therapy, rarely occurs with warfarin and high INR. In the present case, bowel necrosis and thrombogenicity are probably due to COVID-19 infection.

## 4. Conclusion

COVID-19-associated coagulopathy is an acquired and multifactorial syndrome that raises many challenges nowadays, and a different mechanism is involved for the thromboembolic event in this infection. Therefore, the use of anticoagulants alone may not prevent thromboembolic events which happened to the patient under study.

## Acknowledgments

We thank our colleagues from the Surgery Ward in Emam Reza Hospital in Mashhad, Iran, who provided insight and expertise that greatly assisted the present study.

## Footnotes

**Conflicts of Interest:** None to declare.
**Funding:** This research did not receive any specific grant.
**Authors' Contributions:** AA: Writing the original draft (lead). Writing, reviewing, and editing (equal). AD: Conceptualization (lead). Writing, reviewing, and editing (equal). Conceptualization (supporting).
**Ethical Approval:** Informed consent was obtained from a friend of the patient under study.

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