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Life-Threatening Gastrointestinal Complication in A Patient with Severe Covid-19 Disease

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Abstract

Coronavirus disease-2019 (COVID-19) is principally a respiratory illness and pulmonary manifestations constitute the main presentations of the disease, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Besides common respiratory symptoms, some COVID-19 patients experience extrapulmonary presentations. Gastrointestinal (GI) arterial thrombotic events are rarely described in patients with COVID-19 without predisposing factors and are associated with increased mortality (40%). We present a case of a rare life-threatening GI complication in a critically ill patient with COVID-19. A 65-years-old Caucasian male was evaluated because of acute abdominal pain after a meal, which started on day 7 of hospitalization. The patient was hospitalized due to severe COVID-19. He had a medical history of arterial hypertension. Physical examination revealed abdominal distension, tenderness mainly in the periumbilical area, and decreased bowel sounds. Computed tomography (CT) and angiography of the abdomen revealed a 60% obstructive thrombus of the aorta, extending from the aortic circuit to the right common iliac artery, including the celiac and superior mesenteric artery. Furthermore, splenic infarction involving 2/3 of the organ, hepatic infarction, and renal infarction were also noted. Low molecular weight heparin (LMWH) at a therapeutic dose was administered along with aspirin at a dose of 100mg per day. After a long-term hospitalization (30 days) our patient recovered and was discharged from the hospital.At a 3-month follow-up, he had no signs or symptoms of mesenteric ischemia. The insidious onset of bowel ischemia symptoms in patients with COVID-19 should include arterial embolism in the differential diagnosis..

Keywords: COVID-19; SARS-CoV-2; Gastrointestinal Complications; Arterial Embolism; Bowel Ischemia

Abbreviations

COVID-19: Coronavirus Disease-2019; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2; GI: Gastrointestinal; CT: Computed Tomography; LMWH: Low Molecular Weight Heparin; PPIs: Proton Pump Inhibitors; CRP: C-Reactive Protein; LDH: Lactate Dehydrogenase; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; RT-PCT: Reverse-Transcriptase–Polymerase-Chain-Reaction; ARDS: Acute Respiratory Distress Syndrome; RAAS: Renin–Angiotensin–Aldosterone System; ACE2: Angiotensin-Converting Enzyme 2; TE: Thromboembolism

Introduction

Coronavirus disease-2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. COVID-19 manifestations are mostly respiratory with complications ranging from mild disease to respiratory failure, while some patients may be asymptomatic [2]. However, a significant proportion of COVID-19 patients experience extrapulmonary presentations [1]. SARS-CoV-2 can affect the cardiovascular system, neurological system, endocrine system, reproductive system, gastrointestinal (GI) system, renal system, integumentary system, psychology, immune and hematology system[1,3]. GI manifestations are presented in 11-74% of COVID-19 patients, a rate that varies across studies from different countries [1,4,5]. Patients with COVID-19 may develop a variety of GI manifestations, which may pre-exist or not be accompanied by respiratory symptoms [6]. GI manifestations include diarrhea, abdominal pain, abdominal distension, constipation, nausea, vomiting, anorexia, and rarely GI bleeding [4].

Critically ill patients with COVID-19 often develop GI complications during their hospital stay, including bowel ischemia, transaminitis, gastrointestinal bleeding, pancreatitis, Oglivie syndrome, severe ileus, extensive hepatic necrosis, and acute acalculous cholecystitis [2,7]. Notably, serious GI complications have been observed in critically ill patients with a higher frequency than critically ill patients without COVID-19 (74 vs 37%) [7].GI arterial thrombotic events are rarely described in patients with COVID-19 without predisposing factors and are associated with increased mortality (40%) [2]. We present a case of a rare life-threatening gastrointestinal complication in a critically ill patient with COVID-19.

Case Presentation

A 65-years-old man, with a medical history of arterial hypertension, presented to the emergency department with 2 days of worsening dyspnea. He had fever, cough, and fatigue during the week before the presentation. The body temperature was 38,4°C, heart rate 85 beats per minute, respiratory rate 23 breaths per minute, and blood pressure 130/80 mmHg.The oxygen saturation was 88% while the patient was breathing ambient air. Arterial blood gas measurements, obtained while the patient was breathing ambient air, were notable for partial pressure of oxygen of 50 mmHg. The patient had no history of abdominal or pelvic surgery. He was a non-smoker and did not use alcohol. Medications included olmesartan and proton pump inhibitors (PPI) occasionally.

Laboratory test results showed high levels of C-reactive protein 178 mg/dL [CRP (reference range, <6)], lactate dehydrogenase 556 U/L [LDH (reference range, 100-248)], slightly elevated liver enzymes [aspartate aminotransferase AST 59 U/L (reference range, 10-37 U/L) alanine aminotransferase ALT 51 U/L (reference range, 10-45)] and normal levels of blood D-dimer 170 ng/ml (reference range, <500). Chest radiography demonstrated patchy bilateral opacities in the lung parenchyma. A reverse-transcriptase–polymerase-chain-reaction (RT-PCR) assay detected the presence of SARS-CoV-2 RNA in a nasopharyngeal swab.The patient was hospitalized and intravenous ceftriaxone,azithromycin, dexamethasone, remdesivir, prophylactic anticoagulation with subcutaneous enoxaparin, and oral famotidine were administered, as well as supplemental oxygen through a nonrebreather face mask at a rate of 15 liters per minute.

During the next 2 days, dyspnea worsened and the rate of supplemental oxygen increased to 100% through a high-flow nasal cannula. On hospital day 7, the patient developed acute abdominal pain after a meal. Physical examination revealed abdominal distension, tenderness mainly in the periumbilical area, and decreased bowel sounds. High levels of blood D-dimer 10.910 ng/ml were noted, as well as severely elevated transaminases (AST 388 U/L, ALT 375 U/L), LDH 1605 U/L, and CRP 311,7 mg/dL. A non-enhanced computed tomography (CT) of the chest revealed severe COVID-19 (Figure 1). Additionally, a contrast-enhanced CT of the abdomen and angiography demonstrated a 60% obstructive thrombus of the aorta, extending from the aortic circuit to the right common iliac artery, including the celiac and superior mesenteric artery (Figure 2). Furthermore, splenic infarction involving 2/3 of the organ, hepatic infarction, and renal infarction were also noted (Figure 3).

Because of arterial embolism, prophylactic doses of subcutaneous enoxaparin were replaced by therapeutic doses (6.000IU twice a day). Aspirin at a dose of 100mg once a day was also administered. Progressively the patient recovered and was discharged after 30 days, with a prescription of an intermediate dose of anticoagulation and aspirin. At a 3-month follow-up, he had no signs or symptoms of bowel ischemia.

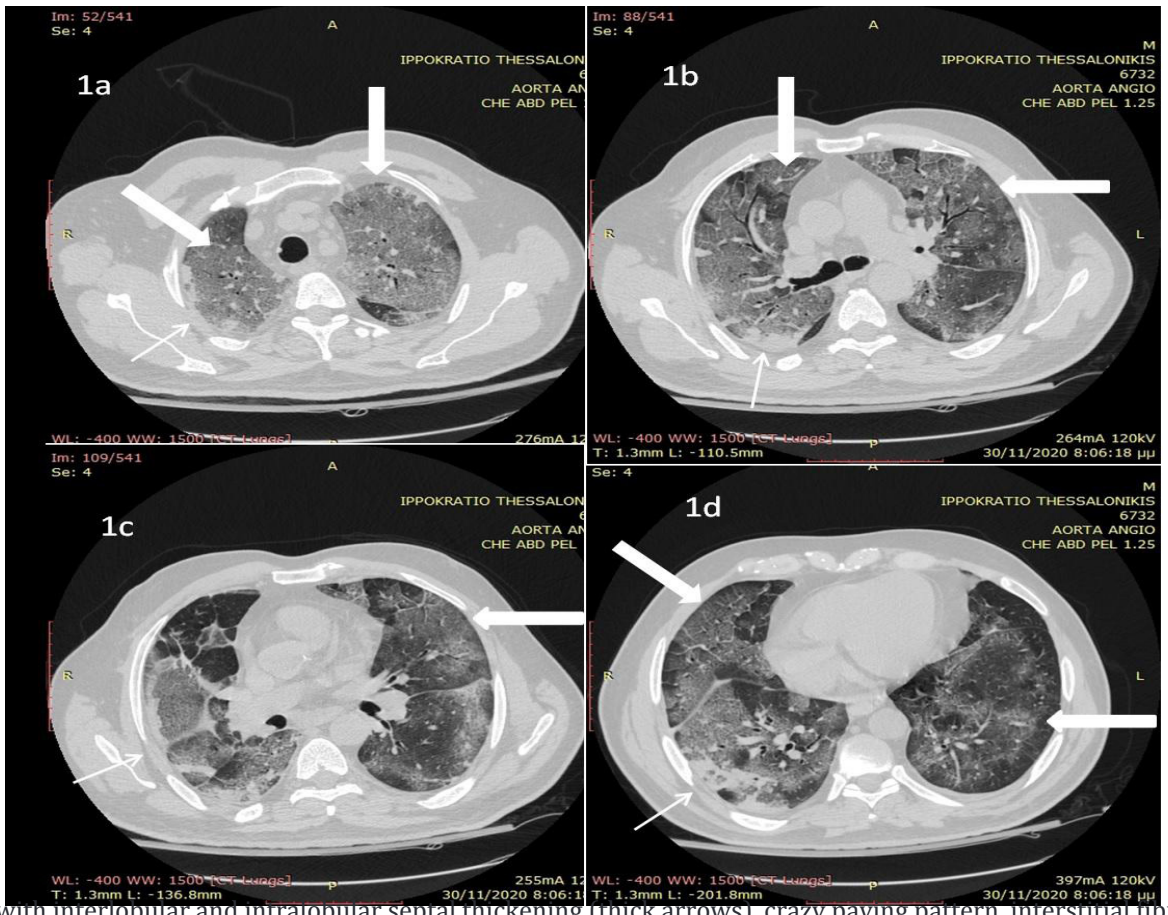

Figure 1: Axial Non-Contrast Chest Computed Tomography Images: multilobar and bilateral severe ground-glass opacities with interlobular and intralobular septal thickening (thick arrows), crazy paving pattern, interstitial fibrosis and atelectasis, more prominent in the right lung (thin arrows), findings suggestive of severe covid-19 disease.

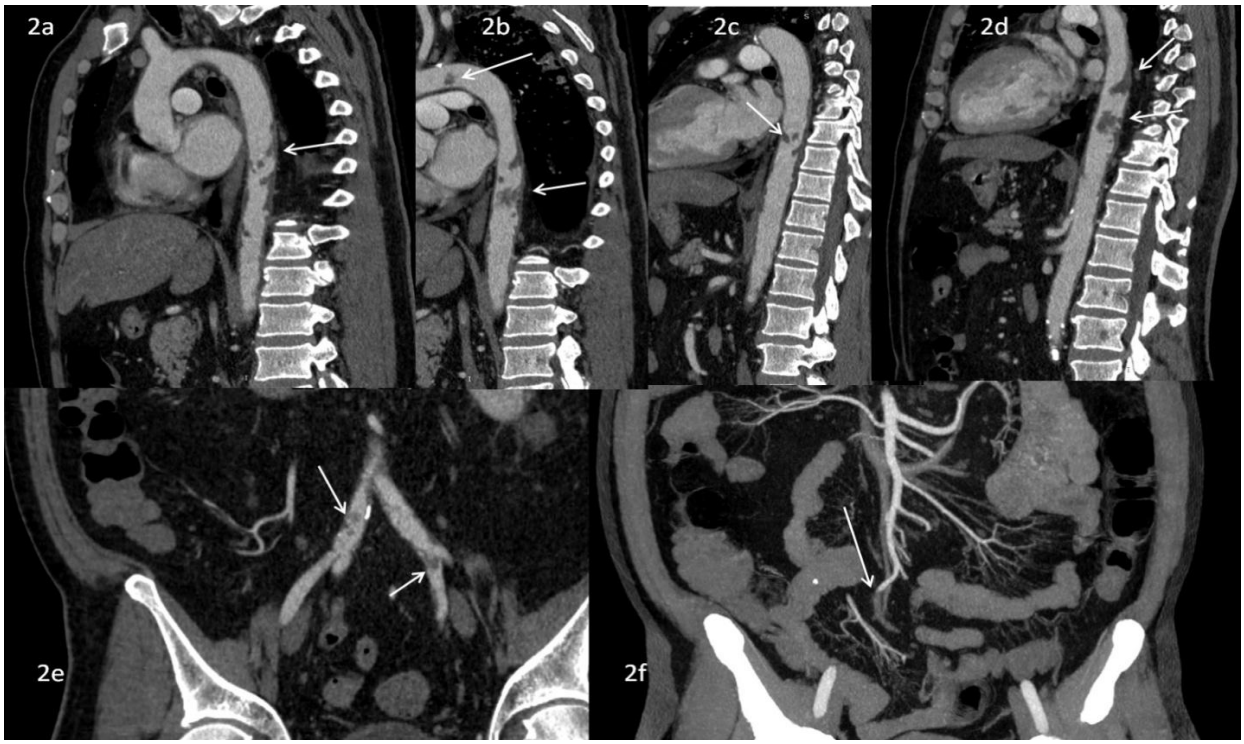

Figure 2: Axial and Coronal Contrast-Enhanced Computed Tomography and Angiography Images: intraluminal filling defect (arrows) in the aortic circuit (b), thoracic aorta (a-d), right common iliac artery and left internal iliac artery (e). A distal branch of the superior mesenteric artery is completely closed by the thrombus (f).

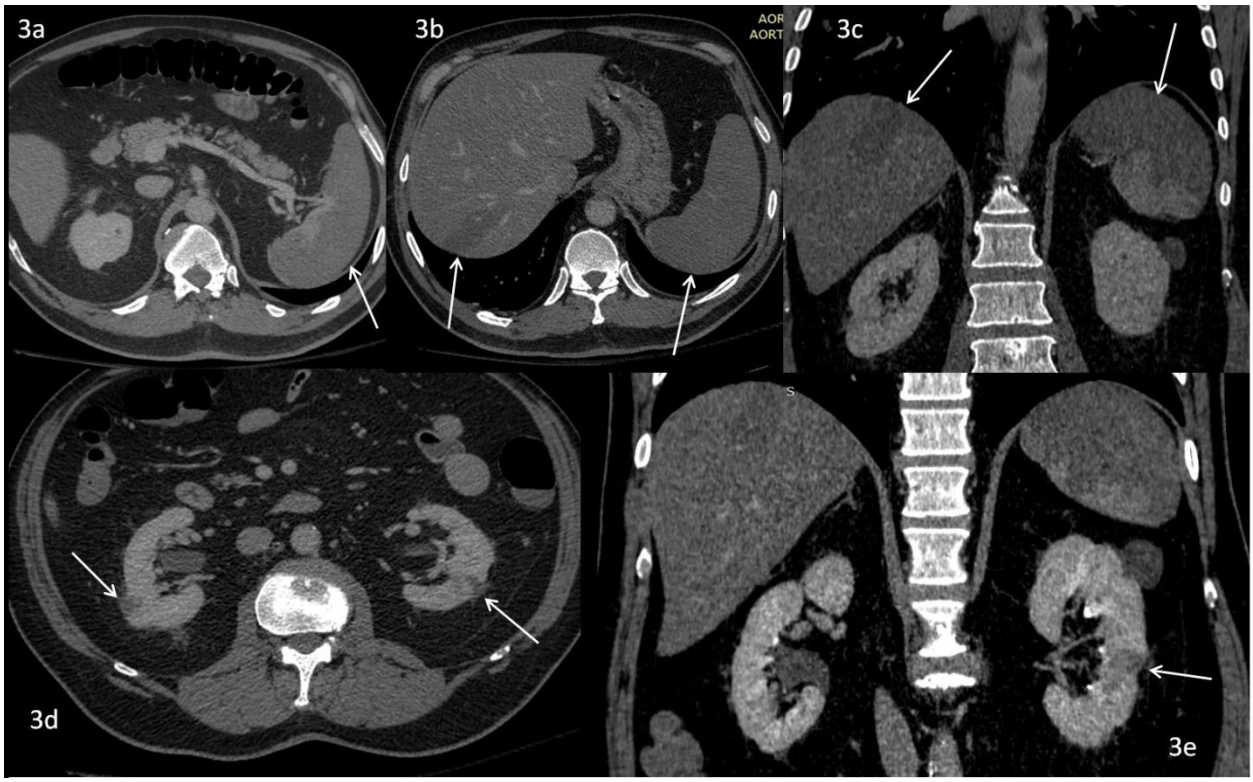

Figure 3: Axial and Coronal Contrast-Enhanced Computed Tomography of the Abdomen: splenic infarction (arrows in images a-c), hepatic infarction (arrows in images b-c) as well as renal infarction (arrows in images d-e).

Discussion

The outbreak of the COVID-19 in Wuhan, China has become the leading cause of respiratory illnesses worldwide. The coronavirus SARS-CoV-2, which is responsible for the COVID-19, causes predominately pulmonary disease, including pneumonia and acute respiratory distress syndrome (ARDS). However, a significant proportion of COVID-19 patients experience extrapulmonary presentations [1-3]. SARS-CoV-2 can affect the cardiovascular system(myocardial injury/ myocarditis, cardiac arrhythmias, Takotsubo cardiomyopathy, cardiogenic shock, myocardial ischemia, acute cor pulmonale, sudden cardiac death, thromboembolic events), neurological system (cerebrospinal fluid infection, Guillain-Barré, stroke, neurological symptoms), endocrine (hyperglycemia, diabetic ketoacidosis), reproductive system (impaired fertility in males and adverse pregnancy outcomes in females), gastrointestinal system (liver dysfunction, gastrointestinal symptoms), renal system (acute kidney injury, proteinuria, hematuria, renal failure), integumentary system (petechiae, livedo reticularis, erythematous rash, urticaria, vesicles, pernio-like lesions), immune and hematology system (blood leukocyte abnormalities, septic shock, disseminated intravascular coagulation, hemophagocytosis) and psychology (anxiety, fear, anger, frustration) [1,3].

Pathophysiological mechanisms that may play a role in multi-organ injury and extrapulmonary manifestations include direct viral toxicity, endothelial cell damage and thromboinflammation, dysregulation of the immune response, and dysregulation of the renin–angiotensin–aldosterone system (RAAS) [1,3,15-17]. However, the exact pathogenetic pathways of COVID-19 are currently not fully understood. Multiple studies have shown that SARS-CoV-2 uses cell receptor angiotensin-converting enzyme 2 (ACE2) to gain cellular access in humans, ACE2 receptors are highly expressed in the lungs, kidneys, GI tract, liver, vascular endothelial cells, and arterial smooth muscle cells. Thus, all these organs might be targets for SARS-CoV-2 infection [1,4,8,9]. SARS-CoV-2 might infect the gastrointestinal tract through its viral receptor ACE2 and there is increasing evidence of a possible fecal-oral transmission route [4,10,15].

COVID-19 is often complicated by coagulopathy with a higher risk of thromboembolism (TE) ranging from 20% to 70%, as in our case [11,12]. In a meta-analysis, the rate of arterial TE was 2% and was associated with increased mortality[11]. Elevated D-dimer is identified as a risk factor for poor prognosis[13]. Critically ill patients with COVID-19 are at increased risk of macrothrombosis (Virchow's triad) and microthrombosis (immunothrombosis related to hypoxemia, endothelial

injury, and inflammation)[14]. Furthermore, the increased expression of ACE2 in endothelial cells after infection with SARS-CoV-2 may perpetuate a vicious cycle of endothelialitis that promotes thromboinflammation [1,4]. However, the detailed pathogenesis of TE in patients with COVID-19 remains unknown. Physicians should be acquainted with embolic events affecting the abdominal organs when asked to consult patients with COVID-19.

A systematic review of ischemic GI complications found that almost half of COVID-19 patients with bowel ischemia had macrovascular arterial/venous thrombosis, as in our case [2]. Overall mortality in those COVID-19 patients was 38% and 40%, retrospectively. The authors concluded that factors such as hypercoagulative state, non-occlusive mesenteric ischemia, and microvascular thrombosis constitute the underlying pathology in the majority of COVID-19 patients with GI ischemic presentation [2].

Conclusion

Arterial thromboembolic events affecting the GI system in critically ill patients with COVID-19 are rarely seen. However, a better awareness of this rare clinical entity and the imaging findings may facilitate early diagnosis. Considering the broad spectrum of clinical manifestations of COVID-19 and the increased mortality rates worldwide, there is an urgent need to rapidly scale up the diagnostic capacity to detect COVID-19 and its related complications. However, further research is needed to better understand the underlying mechanisms linking SARS-CoV-2 with the occurrence of multiple extrapulmonary complications. Our case suggests that the insidious onset of bowel ischemia symptoms in patients with COVID-19 should include arterial embolism in the differential diagnosis.

Author's Contributions

Liava Christina conceived the scientific idea, designed the manuscript, contributed to the analysis and interpretation of the data, and approved the final version of the article. **Petroula Binou** conceived the scientific idea, designed the manuscript, contributed to the analysis and interpretation of the data, drafted the article, and approved the final version. **Angelos Baltatzidis** and **George Sapouridis** contributed to the analysis and interpretation of the data and approved the final version of the article. **Emmanouil Sinakos** conceived the scientific idea, designed the manuscript, contributed to the analysis and interpretation of the data, drafted the article, revised critically the article for important intellectual content, and approved the final version. All authors critically revised the manuscript, approved the final version to be published, and agree to be accountable for all aspects of the work.

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