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Small bowel ischemia and SARS-CoV-2 infection: an underdiagnosed distinct clinical entity

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Introduction

Gastrointestinal symptoms have been described in up to 39% of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infected patients.[1] Evidence for SARS-CoV-2 gastrointestinal infection was already demonstrated in a series of 73 patients, with 53% of patients tested positive for SARS-CoV-2 RNA in stool, possibly by the mediation through the viral host receptor ACE2, which stained positive in the cytoplasm of gastrointestinal epithelial cells.[2] This data suggest that the virus can actively replicate in the bowel, but the computed tomography (CT) rendering of the gastrointestinal infection and its significance for the natural history of the disease remain unclear.

This is a retrospective case series of 3 SARS-CoV-2 infected patients who developed an acute abdomen during the coronavirus disease 2019 (COVID-19) outbreak in Strasbourg (France) in March 2020.

The lack of knowledge concerning CT findings of SARS-CoV-2 gastrointestinal infection and the prognosis of such findings presented a challenge when deciding whether or not to operate these highly frail patients.

Brief clinical report

The patients included a 28-year-old woman (Patient 1), and 2 men aged 56 and 67 years (Patient 2 and Patient 3, respectively). Their medical history was the following: none for patient 1 (P1); high blood pressure, obesity (body mass index of 39), and diabetes for patient 2 (P2); and chronic bronchitis, diabetes, and cardiac transplantation for patient 3 (P3). Patient medication included the following: none (P1); metformin hydrochloride, atorvastatin, and candesartan (P2); and mycophenolate mofetil, everolimus, valsartan, perindopril, pravastatin, insulin aspart, and insulin detemir (P3).

Acute abdomen was inaugural in P1, with abdominal pain and vomiting. Clinical examination showed abdominal guarding. Abdominal CT scan was performed and showed superior mesenteric and portal vein thrombosis and no sign of ischemia (Fig 1, *A*). There were also signs of segmental portal hypertension with gastric varices and portal cavernoma evocative of a previous episode of thrombosis. Anticoagulation was started, with an initial good evolution, followed by a sudden increase in abdominal pain and generalized abdominal contracture on day 5 of the medical treatment. There was no respiratory sign at this point in the evolution. Abdominal CT scan was performed, demonstrating segmental small bowel ischemia (Fig 1, *B*).

Emergency surgery was performed, confirming an 80 cm long jejunal ischemia. Bowel resection and temporary laparostomy were

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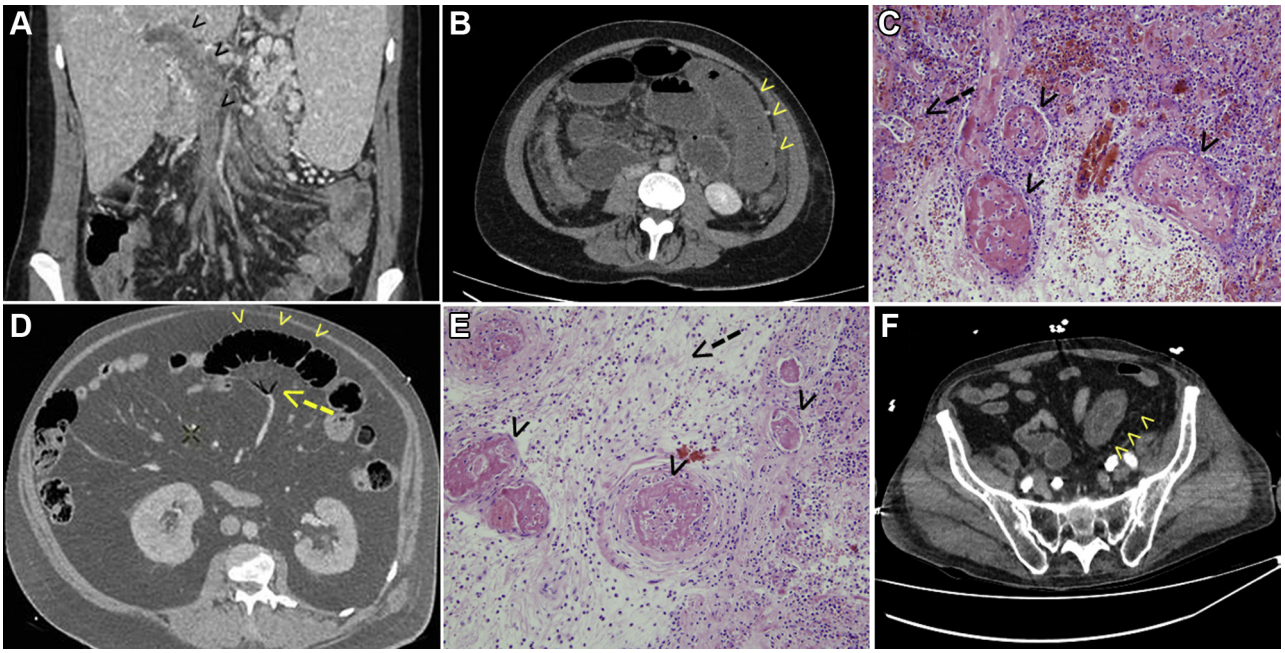

Fig 1. Abdominal CT scan and pathological findings in SARS-CoV-2 infected patients. (*A*) CT scan shows mesenteric and portal vein thrombosis (arrowheads) in a young female patient (P1) with essential thrombocythemia, as a first sign and prior to respiratory symptoms revealing the COVID-19. (*B*) CT scan shows bowel infarction in the first bowel loop (arrowheads) 5 days after admission of the P1, prompting emergency laparotomy and bowel resection. (*C*) Pathological findings of P1 (hematoxylin and eosin stain, 200 × magnification): small bowel necrosis; arrowheads show microthrombi in the lamina propria and the submucosa; arrow shows glandular necrosis. (*D*) CT scan shows signs of bowel ischemia (arrowheads) and mesenteric venous gas (arrow) in the proximal jejunum in a 56-year-old male patient (P2) with acute respiratory distress syndrome during COVID-19. (*E*) Pathological findings of P2 (hematoxylin and eosin stain, 200 × magnification): small bowel necrosis; arrowheads show micro-thrombi; and arrow shows edema and inflammatory infiltrates in the submucosa. (*F*) CT scan shows an inflammatory bowel loop with thickening and edema (arrowhead) in a 67-year-old male patient with acute respiratory distress syndrome during COVID-19. (Color version of the figure is available online.)

performed. A second-look procedure was performed 48 hours later and allowed for a double jejunostomy and abdominal wall closure. The postoperative course was complicated by an acute respiratory distress syndrome on day 1 and SARS-CoV-2 infection was diagnosed. The evolution in the intensive care unit (ICU) was subsequently good, and the patient was discharged from ICU on day 7. The diagnosis of essential thrombocythemia was established. Pathologic findings confirmed the presence of transmural necrosis with several thrombi in the lamina propria and in the submucosa (Fig 1, *C*). The patient was discharged on postoperative day 17.

Patients 2 and 3 were admitted for acute respiratory distress syndrome. The SARS-CoV-2 infection was confirmed on admission both by means of reverse transcription polymerase chain reaction from nasopharyngeal swabs and thoracic CT scan, which demonstrated bilateral viral pneumonia. They were admitted to the ICU and intubated rapidly. After an initial good evolution, both patients presented with a brutal degradation, multiple organ failure, and hemodynamic instability necessitating high doses of noradrenalin, respectively on day 9 (P2), and on day 6 (P3) from ICU admission. The abdominal clinical exam was nevertheless normal (of note, patients were under sedation and curare). CT of the abdomen and thorax was performed.

In patient 2, CT findings were suggestive of ischemia of the first bowel loop, with mesenteric venous gas. However, a permeable arterial axis was observed (Fig 1, *D*). Emergency surgery was performed. The bowel was thickened on a 30 cm long bowel loop, which was centered by 2 areas of transmural necrosis. Bowel resection and laparostomy were performed. A second-look procedure and double ostomy were performed 48 hours later. Pathologic findings confirmed the inflammatory necrosis of the mucosa, which was completely replaced by phantom cells. Several blood clots were seen in the lamina propria and in the submucosa, and the parietal layers were dissociated owing to edema and inflammatory infiltrates (Fig 1, *E*). The postoperative course was slowly favorable, despite the presence of acute renal failure necessitating dialysis. P2 was still in the ICU at the time of manuscript submission.

In P3, CT scan findings were suggestive of an inflammatory segmental ileitis with a localized thickening of 1 small bowel loop and edema (Fig 1, *F*). Decision to continue medical treatment and not to perform exploratory laparotomy was made for P3, not only based on the CT findings suggestive of an uncomplicated bowel inflammation, but also on his burdened medical history and respiratory status. The evolution led to exitus in the next 24 hours.

Discussion

This study describes the clinical and the CT features of 3 patients presenting with an acute abdomen induced by SARS-CoV-2 infection. In 2 patients, the clinical exam was strictly normal, and this did not exclude major bowel complications. This suggests that abdominal CT should be systematically performed in patients with an unexplained degradation of their status after an initial good evolution.

In P1, the mesenteric and portal vein thrombosis shown by the first CT was followed by intestinal transmural necrosis a few days later, in spite of effective anticoagulation. In patients 1 and 2, the presence of micro-thrombi and inflammatory infiltrates seemed to be at the origin of the ischemic event, as the rest of the bowel was strictly normal (ie, with no sign of generalized low flow). Consequently, questions are raised regarding the natural history of bowel inflammation towards ischemia in the presence of SARS-CoV-2

infection. COVID-19 might also favor a hypercoagulation status, thrombi formation, and ischemia, as recently advocated for the etiology of acro-ischemia.[3] Mucosal ischemia might further induce a massive spread of the viruses from the bowel epithelium,[2] and this could be the cause of the patients' deterioration. This assumption should be further investigated.

In conclusion, however, these findings advocate for a reactive approach with early abdominal CT in patients with unexplained worsening status during COVID-19. Exploratory laparotomy and potentially bowel resection should be further considered, if signs of small bowel involvement are detected.

Conflict of interest/Disclosure

All authors declare that they have no conflicts of interest.

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