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COVID-19 Patient Presenting with Total Pancreatic Necrosis and Pancreatico-Colonic Fistula

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Background	The COVID-19 virus has impacted people around the globe, with over 4.5 million deaths related to the virus as of August 2021. Numerous reports have linked COVID-19 to the development of acute pancreatitis. The virus interacts with the pancreas through a variety of mechanisms including the direct binding of the virus through ACE2 receptors.
Summary	A 71-year-old male with multiple comorbidities presented with COVID-19 pneumonia requiring intubation and acute necrotizing pancreatitis with pancreatico-colonic fistula. The patient was critically ill and managed surgically with pancreatic necrosectomy and take-down of the pancreatico-colonic fistula. The patient remained critically ill and ultimately passed away eight days after presentation.
Conclusion	This patient's presentation of severe acute necrotizing pancreatitis secondary to COVID-19 infection and his clinical course progressed similarly to severe acute pancreatitis. COVID-19 is a complex virus with multiorgan tropism, and we are only just beginning to understand its extrapulmonary manifestations.
Key Words	COVID-19; acute pancreatitis; pancreatic necrosis; pancreatico-colonic fistula; pancreatic necrosectomy

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Case Description

The patient, a 71-year-old male with a past medical history significant for end-stage renal disease on hemodialysis, diabetes mellitus (DM), and BMI of 31, presented in October 2020 with acute hypoxic respiratory failure due to COVID-19. He felt ill and reported abdominal pain and distension for one day prior to presentation. He was exposed to COVID-19 in the facility by multiple family members who later tested positive for the virus.

The patient had an extensive cardiac history, including coronary artery disease requiring three-vessel coronary artery bypass in 2017, atrial fibrillation on apixaban, recent non-ST elevation myocardial infarction, and ventricular fibrillation arrest in July 2020 requiring implantable cardioverter-defibrillator (ICD) placement.

The patient was seen and evaluated for acute cholecystitis in September 2020. A cholecystostomy tube was placed due to the high risk of surgery with his recent cardiac arrest. He was discharged to a nursing facility after 20 days. A cholecystostomy tube study showed patent cystic ducts and CBD with no evidence of retained stones.

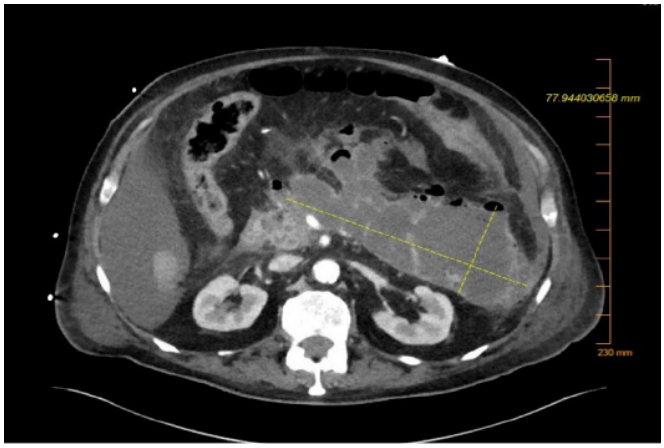
When the patient re-presented October 2020 in the emergency department, he was afebrile but hypotensive and tachycardic. Admission labs were significant for elevated white blood cell count and acute hypoxic respiratory failure (Table 1). He required intubation and was started on vasopressors, intravenous fluids, and antibiotics. His chest radiograph showed interstitial edema and pneumonia. General surgery was consulted for worsening abdominal distension and lactic acidosis. His abdomen was soft, massively distended on physical exam, with no rebound, guarding, or peritoneal signs. Gallbladder etiology was considered initially as his source of pancreatitis; however, he did not previously have elevated lipase or imaging findings of pancreatitis and had a cholangiogram negative for retained stones in the interim.

Table 1. Lab Values at Admission

Admission Labs	
Na	137
K	4.5
Cl	102
CO2	27
Anion Gap	12
BUN	34
Cr	3.75
Glu	149
Ca	7.9
Mg	2
Alk	147
Albumin	1.8
Total Protein	8
Globulin	6.2
AST	39
ALT	13
Bilirubin T	0.9
Amylase	Not evaluated
Lipase	Not evaluated
proBNP	19,566
Total CK	32
Troponin I	0.12
WBC	25
RBC	3.13
Hgb	8.1
Hct	28.4
Platelet	194
pH	7.35
pCO2	46 mmHg
pO2	60 mmHg
Hgb A1c	10.8

Computed tomography (CT) abdomen and pelvis without contrast performed about four hours after arrival to the ED showed extensive pancreatic parenchymal necrosis. An initial scan was unable to localize the fistula, which was thought to be from the duodenum versus the splenic flexure colon (Figure 1).

Figure 1. CT Abdomen Pelvis Showing Extensive Pancreatic Parenchymal Necrosis with Loculated Fluid Collection Measuring 18.8 × 7.8 × 7.2 cm. Published with Permission



Repeat CT abdomen and pelvis with oral was performed to localized fistula and guide surgical planning. This showed contrast extravasation into pancreatic collection (Figure 2) with a fistulous connection to the splenic flexure of the colon (Figure 3). MRCP was considered for evaluation, but the patient was too unstable for the MRI and would not change our treatment plan at this time.

Figure 2. CT Abdomen Pelvis with Oral Contrast Showing Extravasation into Pancreatic Necrosis. Published with Permission

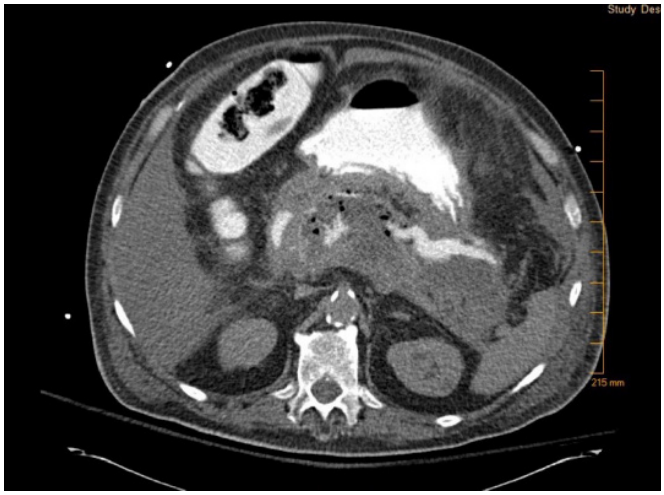
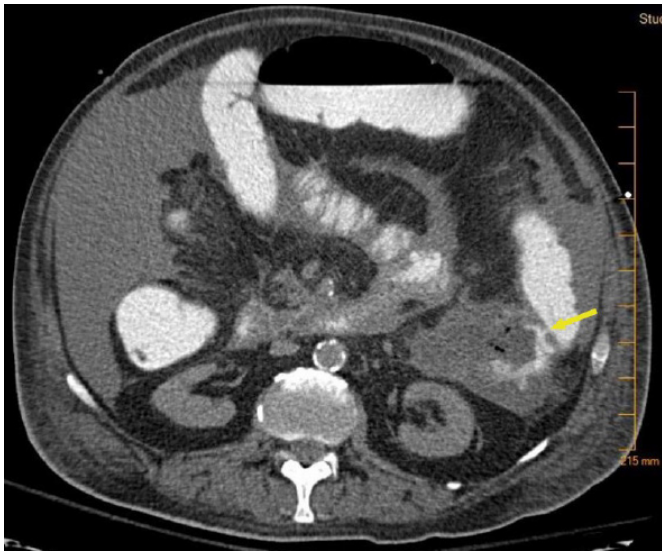


Figure 3. CT Abdomen Pelvis with Oral Contrast Showing Fistulous Connection to Splenic Flexure of the Colon (Yellow Arrow). Published with Permission



Interventional radiology drainage of infected pancreatic necrosis was delayed due to concern for bleeding risk from apixaban. The patient remained in septic shock requiring vasopressors but was stable from a pulmonary standpoint, on minimal ventilator settings.

After extensive discussion with the family, the patient was taken to the operating room for an exploratory laparotomy approximately 24 hours after admission. Precautions were taken in the operating room, including staff use of N95 masks. Careful specimen handling with appropriate protective equipment and a closed suction system was utilized. Eight liters of serous ascites fluid were removed. The lesser sac was obliterated, with the pancreas densely adherent to the stomach and colon. The splenic flexure and descending colon were mobilized, which revealed full-thickness necrosis of the entire body and tail of the pancreas with capsule adherent to the colon. A 1 × 1 cm fistula between the splenic flexure of the colon and pancreas was identified. The segment of colon with the pancreatic fistula was excised using a GIA stapler and sent for pathology. Pathology later showed a disruption of the mucosa in that segment of the colon. The pancreatic tissue sent for pathology showed extensively necrotic tissue with no viable pancreatic tissue identified. The pancreatic body and tail were extensively debrided. Two 19 French drains were placed in the pancreatic bed and left paracolic gutter. The colon was left in discontinuity for planned second-look laparotomy. Hemo-

stasis was achieved at the end of the case. A temporary abdominal closure was performed with a negative pressure device, with a plan to return for a second-look laparotomy.

Immediately postoperatively, the patient became hypotensive and tachycardic to 180 bpm. He received multiple shocks by his ICD for ventricular tachycardia with intermittent atrial fibrillation/flutter. He was started on an amiodarone drip and maximal dosing of four vasopressors. He became coagulopathic with large volume bleeding from his intra-abdominal drains, requiring multiple blood product transfusions. A bicarbonate drip was started for persistent metabolic acidosis. Over the next 24 hours, he developed shock liver. His coagulopathy and bleeding improved, and his vasopressors were weaned. He remained on minimal ventilator settings with 35% FiO2.

A second-look laparotomy was performed two days later. Four liters of old blood and clot were evacuated, but no active bleeding was identified. The transverse colon, proximal to the staple line from the prior colectomy, appeared viable. A right upper quadrant transverse end colostomy was made. The pancreatic bed did not show any bleeding or further pancreatic necrosis. The patient tolerated this procedure well.

The patient continued to improve over the next two days. His vasopressor requirements remained stable, but he could not tolerate hemodialysis due to hypotension. He remained stable on minimal ventilator requirements and 40% FiO2. His colostomy began functioning.

Six days after his initial surgery, the patient acutely decompensated and became hypotensive, requiring four vasopressors with worsening lactic acidosis. There was no evidence of acute intraabdominal process or recurrent bleeding. He developed worsening lung function and shock liver. After extensive multidisciplinary discussion, the family elected to transition to comfort care, and the patient expired eight days after the initial presentation.

Discussion

As of August 2021, there have been over 261 million confirmed cases of COVID-19 worldwide, with 4.5 million related deaths,[1] of which there have been 637,385 related to COVID-19 in the United States alone.[2] Links between COVID-19 infection and acute pancreatitis (AP) development have been described in the literature in case reports and small series.[3–5]

This patient's initial presentation of acute necrotizing pancreatitis was atypical in its severity and acuity of onset. Since he had just undergone percutaneous cholecystostomy drainage without stones visualized on follow-up imaging, it is unlikely his pancreatitis was related to gallstones. His initial COVID-19 respiratory symptoms required intubation but did not progress to acute respiratory distress syndrome (ARDS). His clinical course appeared consistent with multiorgan dysfunction syndrome (MODS) secondary to acute pancreatitis (AP) rather than COVID-19 pneumonia.

The SARS-CoV-2 virus enters host cells via the spike protein, which binds to angiotensin-converting enzyme 2 (ACE2) receptors on the cell surface. The virus binds to the ACE2 receptor on the lung's type 2 alveolar cells leading to progressive viral pneumonia and ARDS. The ACE2 receptor is also expressed in the esophagus, ileum, colon, heart, kidney, adipocytes, and pancreas leading to the multiorgan tropism seen with COVID-19 infection.[5] There are multiple proposed mechanisms for pancreatic injury during COVID-19 infection. Direct virus-mediated injury of the exocrine pancreas and islet cells through ACE2 receptors. Additional secondary pancreatic injury due to virus-induced lipotoxicity, severe COVID-19 infection cytokine storm and MODS, and drug-induced pancreatic injury (NSAID, steroids).[5]

AP has been described as presenting and primary symptom of COVID-19 in patients as young as seven,[6] both with and without respiratory involvement.[5] Autopsy reports identified pancreatic injury at higher rates than clinically evident pancreatitis.[5] Higher rates of idiopathic pancreatitis were reported in COVID-positive patients.[5] One case described a patient with AP and small bowel fistula requiring surgery who was diagnosed with COVID-19 after presentation.[7] There are reports of "acute diabetes," new-onset DM in COVID-19 patients, and worse clinical outcomes in patients with preexisting DM.[5,8] Akarsu et al. reported AP in 12.6% of patients admitted with COVID-19 pneumonia, with a 32.5% incidence in critically ill patients.[9] AP was associated with higher mortality rates secondary to COVID-19 pneumonia.[9]

Though endoscopic or percutaneous drainage is preferred for ANP, there is no clear guidance for the use of endoscopic treatment in the setting of a pancreatic fistula.[10–12] This patient was also unable to undergo percutaneous drainage due to his anticoagulation and cardiac history. Though rare, Pancreatico-colonic fistulas can occur in as many as 3 to 10% of cases of severe acute pancreatitis.[12] To identify

these fistulas radiographically, CT with or without contrast is preferred.[12] In these cases, definitive treatment with surgical resection of the involved portion of the colon with possible pancreatectomy and drainage of the pancreatic area is recommended.[12]

Conclusion

COVID-19 is a complex virus with multiorgan tropism, and we are only just beginning to understand its extrapulmonary manifestations. The virus interacts with the pancreas through a variety of mechanisms. The clinical and surgical manifestations of COVID-19-induced acute pancreatitis still need further investigation.

Lessons Learned

Surgeons should be aware of extrapulmonary manifestations of COVID-19, including severe acute pancreatitis. COVID-19 may also worsen the course of other etiologies of pancreatitis through additional pancreatic injury. The step-up method for managing acute pancreatitis should continue to be utilized at this time for COVID-19-related acute pancreatitis.

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