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Case Report

Necrotizing pancreatitis in a COVID-19 patient managed with endoscopic AXIOS stent placement

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ABSTRACT

As coronavirus disease 2019 (COVID-19) is a relatively novel infectious process, atypical presentations like acute pancreatitis (AP) are still being studied and a clear association between pancreatic injury and severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has yet to be established. This makes the diagnosis and management of such conditions exceedingly difficult. Although several cases of severe AP with concurrent SARS-CoV-2 infection have been reported, to the best of our knowledge, ours is the first COVID-19 case to present with necrotizing pancreatitis and the first reported case requiring intervention for associated local complications.

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Keywords: Coronavirus; COVID-19; Endoscopy; Pancreatitis, acute necrotizing; Stents

Introduction

The current coronavirus disease 2019 (COVID-19) pandemic has proven to be a significant challenge to both public health and clinical medicine. Having affected more than 54 million people and causing more than 1.3 million deaths in 2020 alone, COVID-19 was the third-leading cause of mortality in the United States in 2020.^{1,2} With the rising number of cases, the involvement of systems other than the respiratory system as part of the spectrum of COVID-19 is becoming more evident. Although viral pancreatitis has been extensively described in the literature, the association between pancreatitis and severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection is poorly defined.³ Here we present the first reported case of necrotizing pancreatitis with concurrent SARS-CoV-2 infection that needed intervention.

Case Report

A 58-year-old male presented to the emergency department with progressively worsening abdominal pain for 1 week associated with nausea and non-bloody emesis. The patient tested positive for COVID-19 1 week prior with symptoms of fever (peaking

at 38.3°C), fatigue, and an altered sense of taste/smell and was treated with steroids and azithromycin. The patient reported drinking alcohol occasionally (1–2 times/month) and had a 30–40 pack-year smoking history but had quit 6 years ago. There was no significant past or family history. Laboratory analysis showed leukocytosis with a left shift (16.5 with 81% neutrophils), mildly elevated creatinine (1.5 mg/dL), elevated lipase (> 5,600 U/L), normal liver tests, serum calcium and triglyceride levels within normal limits, and a positive COVID-19 reverse-transcription polymerase chain reaction test. Abdominal ultrasound demonstrated gallstones but was negative for choledocholithiasis and acute cholecystitis. Computed tomography (CT) demonstrated acute uncomplicated pancreatitis and the patient was admitted for supportive care. A follow-up CT scan performed 2 days later showed necrotizing pancreatitis with worsening inflammation, pancreatic and peripancreatic necrosis, and early acute necrotic collections, as well as small bilateral pleural effusions, and scattered ground-glass opacities (Fig. 1). Magnetic resonance cholangiopancreatography (MRCP) further confirmed necrotizing pancreatitis with hemorrhage/proteinaceous debris (Fig. 2). The patient was managed conservatively with aggressive intravenous hydration (30 mL/kg/day for 24 hours followed by goal-directed hydration), an-

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timicrobials (piperacillin-tazobactam transitioned to meropenem and fluconazole), morphine and hydromorphone for pain control, and anti-emetics. He was also started on remdesivir and convalescent plasma in view of his COVID-19 infection. The patient tolerated a regular diet, did not have any fluid overload symptoms and was discharged in a stable condition after the completion of treatment.

The patient presented 20 days later with fever, decreased ap-

petite, nausea, early satiety, and worsening fatigue. The lipase level was 38 U/L and liver tests were unremarkable. CT showed a 12-cm intra- and extra-pancreatic infected necrotic collection containing fluid, debris, and gas consistent with infected walled-off necrosis (Fig. 3). The patient was admitted and started on intravenous fluids, meropenem, and fluconazole. MRCP showed walled-off necrosis replacing the majority of the pancreatic body. Due to the persistent symptoms, the patient underwent endoscopic ultrasound (EUS) for AXIOS drainage. EUS showed diffuse moderate mucosal changes characterized by congestion in the entire duodenum. A hypoechoic, multicystic, septated lesion was identified in the pancreatic body (Fig. 4). A cystogastrostomy was performed using the AXIOS stent system. The patient showed significant improvement in symptoms following EUS and was discharged home with 4 weeks of meropenem. We suspect that

Fig. 1. Axial contrast-enhanced computed tomography image demonstrating acute necrotizing pancreatitis. Parenchymal necrosis is seen as areas of nonenhancement in the pancreatic head (arrow) relative to normal enhancing pancreatic tissue more posteriorly (arrowhead). There is associated peripancreatic inflammatory stranding in the bilateral retroperitoneum and mesentery, as well as early acute necrotic collections (asterisk).

Fig. 2. Noncontrast coronal T1-weighted fat-saturated image showing diffusely abnormal pancreatic and peripancreatic signals from necrotizing pancreatitis. Areas of T1 hypointensity in the head (arrow) correspond to areas of normal pancreatic enhancement on computed tomography (CT), while areas of abnormal markedly hyperintense signals in the neck and body (arrowheads) correspond to areas of non-enhancement on CT and reflect hemorrhagic and proteinaceous debris from necrosis. Note the T1 heterogeneous early acute necrotic collection (asterisk).

Fig. 3. Axial contrast-enhanced computed tomography showing development of a 12-cm infected walled-off necrosis containing air, fluid, and debris (arrows). There is new dilation of the common bile duct due to downstream obstruction by the inflammatory process (arrowhead).

Fig. 4. Endoscopic ultrasound demonstrating a hypoechoic, multicystic, septated lesion within the body of the pancreas compatible with walled-off necrosis (arrows).

COVID-19 was the cause of acute pancreatitis (AP) in this patient based on the temporal association.

Informed consent was obtained from the patient during an outpatient visit and was again obtained telephonically.

Discussion

The full spectrum of the disease caused by COVID-19 is still being studied, with new symptoms being reported in different organ systems. AP cases associated with COVID-19 have been reported in the literature. SARS-CoV-2 enters the host cells via angiotensin-converting enzyme 2 receptors. These receptors are highly expressed in both the exocrine tissue and endocrine islets of the pancreas, making them a potential target for the virus.³ Although the exact pathogenesis is not known, there are a few possible mechanisms of pancreatic injury in COVID-19 infection, as follows: 1) direct cytopathic effects of local viral replication, 2) injury due to the systemic immune response induced by the virus, 3) drug-mediated pancreatic injury (nonsteroidal anti-inflammatory drugs, steroids, tocilizumab, etc.), 4) endothelial injury leading to ischemia by causing thrombosis, and 5) hypoperfusion.²

The diagnosis of COVID-19-associated pancreatitis can be difficult. One reason is that patients may have other risk factors for AP, such as alcohol abuse and cholelithiasis, and concurrent medication use. It can be challenging to completely exclude these factors. Our patient did have cholelithiasis and had been treated with azithromycin and steroids, both of which have been associated with drug-induced pancreatitis.⁴ Although he had no liver function test (LFT) abnormality during disease onset, this cannot exclude cholelithiasis as a potential etiology for AP, as about 15% to 20% of acute biliary pancreatitis patients have normal LFTs.⁵ Although drug-induced pancreatitis is very uncommon and only accounts for 0.5% to 2% of all cases, it has to be considered in every single case. Drugs that are known to cause pancreatitis as an adverse event include oral contraceptives, statins, diuretics, anti-retroviral agents, anticonvulsants such as valproate, and some of the newer immune checkpoint inhibitors, especially CTLA-4 inhibitors or when used in combination.^{6,7} However, most cases of drug-induced pancreatitis are very mild, and the symptoms improve immediately after stopping the medications, which was not seen in our case. Another factor adding to the difficulty of the diagnosis is that pancreatic enzyme elevation can occur in many other conditions besides AP, especially in the presence of renal or respiratory failure, which can be commonly encountered in COVID-19 cases.⁸ Two recent studies showed a 17% incidence of elevated serum lipase and amylase in patients with COVID-19 pneumonia.^{3,9} In a study following 71 patients with COVID-19 and elevated lipase levels (> 3 times the upper normal limit), only 15 patients were actually diagnosed with AP.¹⁰ The third reason is that abdominal pain, nausea, and vomiting are relatively non-specific and can be attributed to the generalized infectious process in a COVID-19 patient, leading to a delay in the diagnosis of AP. The revised Atlanta classification should be used to make the diagnosis of AP irrespective of the presence or absence of concomitant COVID-19.¹¹

Pancreatic injury in COVID-19 can range from an isolated elevation in pancreatic enzymes to a classic episode of AP.⁸ De-Madaria and Capurso² applied the Bradford-Hill causality criteria framework and concluded that strong plausibility, coherence, and strength exist. Autopsy data also suggests that the incidence of AP is higher than that diagnosed clinically.¹² There is a clear increment in mortality in AP patients with concurrent COVID-19 infection,¹³ stressing the need for separate management guide-

lines. A recent study comparing the clinical outcomes in patients with AP with and without concomitant COVID-19 concluded that patients with associated COVID-19 had a higher incidence of persistent organ failure (odds ratio [OR] = 2.77), prolonged hospital stay (OR = 1.32), and 30-day mortality (OR = 2.41).¹⁴ Intravenous hydration remains the cornerstone of therapy for AP but concurrent respiratory and renal failure in the setting of COVID infection makes worsening of pulmonary edema a major concern. The Society of Critical Care Medicine recommends conservative rather than aggressive fluid replacement, even in the setting of shock.¹⁵ As demonstrated in our case, decompensation may also occur after the initial resolution of symptoms, possibly due to the persistence of the viral load. This makes the thorough follow-up with a clinical, laboratory, and radiological evaluation extremely important.

At present, there is no concrete evidence of an association between SARS-CoV-2 and AP. However, the rising number of reports describing in the setting of COVID-19 warrants more studies to examine the possibility of an acausal relationship. The diagnostic dilemma, aggressive clinical course, limitations in the liberal use of intravenous fluids, and the possible presence of the virus in local tissues make the development of severe AP in concurrent COVID-19 infection “double-trouble” for both the patient and the physician. Proper diagnostic protocols and management algorithms need to be put in place for these patients with a special emphasis on early recognition and management of local complications.

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Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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