# **Case Report**

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# A serendipitous case report of acute pancreatitis complicated by pseudocyst in a patient with COVID-19

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#### **ABSTRACT**

Acute pancreatitis is a common gastrointestinal disease, most frequently requiring acute hospitalization. During SARS-CoV-2 (severe acute respiratory syndrome coronavirus-2) pandemic, the etiologic agent of COVID-19, several studies described the involvement of other tissues besides the respiratory tract, such as the gastrointestinal tract. In pancreas, ACE-2 receptor is expressed in exocrine glands and islets, both being targets for the virus and subsequent pancreatic injury. There are few articles which report pancreatic injury in COVID-19 patients but most of them do not report acute pancreatitis. Diagnosing acute pancreatitis in the setting of COVID-19 pandemic is challenging and requires ruling out all other potential causes of pancreatitis. Herein we report a rare case of severe acute pancreatitis.

Keywords: COVID-19, SARS-CoV-2, Acute pancreatitis, Pseudocyst

## INTRODUCTION

SARS-CoV-2 (severe acute respiratory syndrome coronavirus-2), the etiologic agent of COVID-19 pandemic, has spread rapidly worldwide since December 2019. Although COVID-19 primarily attacks the respiratory system, new clinical manifestations emerge everyday and should not be neglected, even the innocuous ones. This is for the better understanding, early recognition and management of such cases. Acute pancreatitis (AP) is an inflammatory disease affecting the exocrine part of the pancreatic parenchyma and is associated with high morbidity and mortality.1 Laboratory abnormalities showing hepatic and pancreatic injury have been evident in a subset of patients, although it remains unclear if these abnormalities have any impact on prognosis.<sup>2</sup> The most common causes of acute pancreatitis are gallstones and alcohol abuse, but viral pancreatitis has been well described in the literature, mainly due to mumps, measles, coxsackia, epstein-barr virus and hepatitis.3 Little is known about the pancreatic lesions caused by SARS-CoV-2 infection. Angiotensin-converting enzyme-2 (ACE2), the functional virus host cell receptor, expressed in both exocrine and endocrine pancreatic cells, plays a role in this disease process. The mechanisms of pancreatic injury in SARS-CoV-2 infection include direct cytopathic effects or indirect systemic inflammatory and immunemediated cellular responses, resulting in organ damage or secondary enzyme abnormalities.<sup>4</sup> The case report discussed here describes a patient with COVID-19 that developed severe acute pancreatitis complicated by pseudocyst.

### **CASE REPORT**

A 40 year old Indian male, non-smoker and non-alcoholic, banker by occupation with no co-morbidities presented to our emergency department with complaints of fever, cough and malaise since 10 days, vague abdominal pain since 10 days which progressed to severe agonizing and excrutiating epigastric pain since last 2 days which was radiating to the back and aggravated on lying supine and relieved on sitting and bending forward, and shortness of breath since 2 days.

No history of any drug intake prior to admission or use of any psychotropic substances. No history of previous similar episodes or any family history suggestive of hypercalcemia, hypercholesterolemia or malignancy. No past history of tuberculosis, rheumatological/connective tissue disorder and no history of any past surgical procedures or trauma.

On general examination, patient was well built and conscious, irritable, febrile, tachypneic with a respiratory rate of 24/min, resting pulse was 136/min and regular, blood pressure was 100/60 mmHg and oxygen saturation SpO<sub>2</sub> of 92% at room air and 99% on 2 L of oxygen via nasal prongs.

On systemic examination, cardiovascular revealed tachycardia but no gallop; neurological was normal; mild crepitations with decreased breath sounds were noted at basal lung fields on respiratory system examination with per abdominal examination revealing epigastric tenderness, guarding and rigidity with no shifting dullness.

Initial laboratory work up done in our hospital revealed haemoglobin of 13.1g/dl, total leukocyte count of 5,260 cells/cumm (normal differential count) and platelet count of 210,000 cells/cumm. Peripheral smear was unremarkable. Erythrocyte sedimentation rate was 40 mm in first hour. Serum ferritin was 836.48 ng/ml, CRP was 147.23 mg/l and LDH was 780 U/l. Coagulation profile was normal with PT/INR- 12.1/1.18, APTT-25.2 and D-dimer- 1.45 mcg/ml. Liver and kidney function tests were within normal limits. Serum electrolytes were normal. Serum calcium and lipid profile (triglycerides- 158 mg/dl) were within normal limits. Serum vitamin B12 and folate levels were normal.

Rheumatoid factor and antinuclear factor were negative. The electrocardiogram showed regular sinus rhythm of 136 bpm with QT at 410 nm without repolarization disorders. The echocardiography showed normal ventricular chambers with a systolic ejection fraction of 60%, no valve abnormality and no signs of pulmonary hypertension or acute or pulmonale. The patient was then tested for COVID-19 on a nasopharyngeal sample using RT-PCR technique, which came out to be positive. Chest radiography showed bilateral, multiple, diffuse reticular changes with HRCT thorax showing multiple subpleural, lobular and peribronchila areas of ground glass opacities with few areas of consolidation in the background of interlobular septal thickening noted in lower segments of lung segments with CT severity score of 20/25 (Figure 1).

In addition to the pulmonary findings, chest CT showed abnormalities of pancreas such as peripancreatic fat stranding around the tail of the pancreas with the main pancreatic duct in the region of the body, measuring 7 mm and a well-defined fluid attenuating hypodense collection of 11.8×11.0×13.3 cm (TR×AP×CC) noted in the region of the tail of the pancreas, extending inferiorly into the left

posterior pararenal space, displacing thw left kidney anteriorly.



Figure 1: Patient's HRCT showing predominantly basal, posterior and subpleural ground glass opacities (GGO) and consolidation with normal cardiac parameters.

The collection is noted extending superiorly into the subphrenic space, elevating the left diaphragm and displacing the spleen inferiorly with all the features suggestive of acute pancreatitis with pseudocyst formation (Figure 2-5).

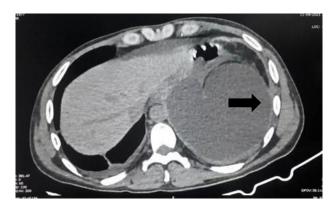


Figure 2: Patient's CT abdomen showing hypodense collection in the region of the tail of the pancreaspseudocyst, a complication of acute pancreatitis.

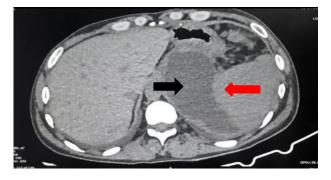


Figure 3: Patient's CT abdomen showing hypodense collection (black arrow) extending superiorly into the subphrenic space, displacing the spleen inferiorly (red arrow).

Serum pancreatic enzymes were measured after the CT findings, which showed amylase and lipase levels to be 3798 U/l and 1915 U/l. His glucose level was varying between 120-180 mg/dl and HbA1C was 5.2%.

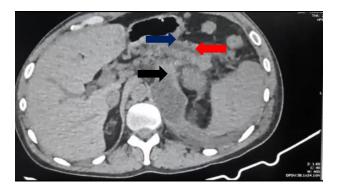


Figure 4: Patient's axial CT abdomen showing tumefied pancreas with loss of its physiological lobulations associated with an infiltration of peripancreatic fat (red arrow), fluid attenuating hypodense pseudocyst (black arrow) and main pancreatic duct measuring 7 mm (blue arrow).



Figure 5: Patient's axial CT abdomen showing hypodense collection (black arrow) extending inferiorly into the left posterior pararenal space, displacing the left kidney anteriorly (red arrow).

The patient was then transferred to the COVID-19 isolation high dependency unit (HDU), put on high flow nasal oxygen (HFNO) and tapered to room air as he improved. He was given antipyretic paracetamol depending on febrile episodes along with tablet azithromycin 500 mg per oral once a day and was also started on injection enoxaparin 60 mg subcutaneous twice a day, injection methylprednisolone 60 mg intravenous once a day and injection remdesivir 200 mg intravenous infusion on day 1 followed by 100 mg intravenous infusion from day 2-5, in concurrence with the local COVID-19 protocol.

In view of CT severity index for pancreatitis score being seven, he was shifted from HDU to ICU and managed conservatively with digestive rest (nil per oral), change to intravenous antibiotic injection piperacillin/tazobactum 4.5 g every 6<sup>th</sup> hourly and adequate hydration and analgesia. A daily decline of amylase and lipase were

observed from day 17, which eventually normalized on day 23 with patient symptomatically better and able to breathe on room air. Other causes of acute pancreatitis such as drugs, gallstones, trauma and hypotension were excluded and the patient was discharged after 30 days of hospitalization when his repeat nasopharyngeal swab RT-PCR came negative and was advised to follow-up every 6 weeks to undergo magnetic resonance cholangiopancreatography (MRCP) and endoscopic ultrasound and to plan surgical procedure if any, at a later date.

#### DISCUSSION

Acute pancreatitis is an inflammatory condition of the exocrine pancreas, caused most commonly by gallstones and alcohol consumption. Acinar cell injury and impaired zymogen secretion leading to intrapancreatic protease activation underlie this disease. Diagnosis requires two out of three criteria: typical history, elevated serum amylase or lipase more than three times the upper limit of normal for the laboratory reference range and suggestive imaging findings.<sup>5</sup> Several viruses have been implicated in the These include aetiology of acute pancreatitis. cytomegalovirus, epstein-barr virus, hepatitis A-E viruses, herpes simplex virus, varicella zoster virus, mumps, measles and coxsackie virus, among others. The exact mechanism by which viruses cause pancreatitis is unknown and each virus might cause pancreatitis through a different mechanism. These mechanisms include viral replication in pancreatic acinar cells resulting in protease leakage and activation, in addition to cholangiopathy and ampullary oedema.6

ACE-2 receptor is abundantly expressed in many different tissues, justifying the involvement of different organs and extrapulmonary symptoms of COVID-19 patients.<sup>7</sup> The expression of ACE2 in the gastrointestinal tract during SARS-CoV-2 infection leads to digestive system dysregulation.4 Symptoms like nausea, vomiting and diarrhea have commonly been described in 11%-50% of cases.8 Gastrointestinal findings are significant due to their association with adverse outcomes from delayed hospital admission and evidence of more laboratory changes, including prolonged coagulation time.9 In addition to gastrointestinal symptoms, some blood abnormalities were found in severe patients, such as increased pancreatic enzymes suggesting pancreatic injury. 10 Therefore, it is likely to consider SARS-COV-2 as a potential cause of pancreatitis. Curiously, in a recent study published by Schepis et al SARS-COV-2 RNA was detected in a pancreatic pseudocyst sample endorsing pancreatic involvement in COVID-19.11

Several cases of pancreatitis in patients with COVID-19 were reported. Gonzalo et al reported a case of pancreatitis from Spain in the absence of the most common risk factors: alcohol and gallstones. <sup>12</sup> Lakshmanan and Malik et al also reported a case of a nursing home resident who tested positive for SARS-CoV-2 following an outbreak at his residence and developed pancreatitis a few days later. <sup>13</sup>

Moreover, Brikman et al reported a case of a patient with COVID-19 pneumonia who developed acute pancreatitis 14 days following admission.<sup>14</sup>

The patient did not have any history of pancreatitis, gallstones or alcohol intake. Further supportive data are provided by Meireles et al in a report of a patient with COVID-19 pneumonia who developed acalculous pancreatitis on the 11th day of the disease in whom other viral causes have been ruled out by laboratory investigations.<sup>15</sup>

ACE2 receptor is highly expressed in pancreatic islet cells and exocrine cells, which being target for SARS-CoV-2 leads to the elevation of both exocrine enzymes, amylase and lipase as well as glucose level dysregulation which can be exacerbated by using certain COVID-19 specific drugs such as dexamethasone/methyprednisolone. <sup>16</sup> In our case, there was three fold elevation in the amylase and lipase levels and also glucose levels were above the accepted range with normal HbA1C suggesting acute event such as COVID-19 affecting both exocrine and endocrine arm of the pancreas which due to delayed presentation lead to the formation of a massive pseudocyst which was managed conservatively leading to discharge and follow-up with good outcome.

To link any casual association between acute pancreatitis and COVID-19, further investigations are required. Acute pancreatitis is a common disease and can often be idiopathic with no identifiable aetiology. Due to COVID-19 being contagious and lack of diagnostics in many centres, pancreatitis can be easily underdiagnosed and treated as other gastrointestinal ailments. Nevertheless, pancreatitis seems to be an uncommon complication of COVID-19.<sup>17</sup> A study from the USA revealed a point prevalence of 0.27% of acute pancreatitis in hospitalised patients with COVID-19.<sup>18</sup> Another study from Spain reported a frequency of 0.07%.<sup>19</sup> Further studies are needed to evaluate the incidence compared with that of pre-COVID-19 times.<sup>17,20</sup>

#### **CONCLUSION**

SARS-CoV-2 seems to have some tropism for pancreatic (exocrine and endocrine) cells, causing acute pancreatitis. However, acute pancreatitis should be diagnosed based on the standard criteria as elevation of pancreatic enzymes is also seen in COVID-19 infection without pancreatitis. Patients with a complicated course, who require invasive procedure might pose risk of transmission to the operating surgeon or interventionist. So, precautionary measures must be taken. Diagnosing acute pancreatitis with pseudocyst formation is important for adequate treatment and better management of systemic repercussions, thus decreasing SARS-CoV-2 mortality.

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