Case Report

# Is SARS-COV-2 a New Trigger of Acute Pancreatitis? A Case Report

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**Abstract**
Although SARS-CoV-2 commonly affects the respiratory system, several other major organ systems can be involved, including the gastrointestinal. The main gastrointestinal manifestations are diarrhoea, nausea, and vomiting. Few cases of acute pancreatitis along with COVID-19 infection have been reported. Current evidence stresses that both clinical and radiographic studies can be suggestive of acute pancreatitis in COVID-19 patients, even without any respiratory symptoms.
We report a case of a female patient who presented with severe epigastric pain and vomiting and was diagnosed with acute pancreatitis on a COVID-19 infection. The patient had an otherwise unremarkable medical history. Upper respiratory symptoms were developed on day 2 of her hospital stay. Acute pancreatitis was attributed to the COVID-19 infection, following the exclusion of other common causes of pancreatitis. Our case points out that acute pancreatitis can be developed in asymptomatic COVID-19-infected patients as well as those with a mild form of COVID-19 infection.

**Key words**: acute pancreatitis, COVID-19, ACE-2 receptor, MRCP, abdominal CT

## Introduction

The binding of SARS-COV-2 to the angiotensin-converting enzyme 2 (ACE2) receptor, which is expressed in multiple organs, allows the virus to enter endothelial cells. (Ni, et al., 2020). Its symptoms, which range in severity from mild fever and cough to more severe ones, are mostly related to the respiratory system. Yet, a number of studies have documented diverse extrapulmonary SARS-COV-2 presentations (Choden, et al., 2023, Onoyama, et al., 2022, Chatzis, et al., 2022). Indeed, the gastrointestinal and hepatobiliary systems are frequently affected, followed by the pancreas and spleen. Abdominal pain, nausea, vomiting, diarrhea, and gastrointestinal bleeding are among the common symptoms (Alves, et al., 2020). Emerging data indicates a causal relationship between SARS-CoV-2 and acute pancreatitis (AP), even though pancreatic involvement is uncommon in COVID-19 patients (Choden, et al., 2023). Acute AP was observed in approximately 0.1% of hospitalized COVID-19 patients (EBiK, et al., 2022). After contracting COVID-19, there is frequently a pancreatic injury that shows up as elevated pancreatic enzyme levels and, in more extreme

cases, as acute pancreatitis (Choden, et al., 2023, Kataria et al., 2020). Recent data indicates that patients with COVID-19 infection and acute pancreatitis had a higher risk of developing moderate to severe acute pancreatitis (AP), as well as a higher risk of death and other complications (Balthazar, et al., 2022). Research also showed that AP is typically followed by respiratory COVID-19 symptoms and can occasionally manifest as either the main COVID-19 presentation or as a separate event devoid of any COVID-19 symptomatology (Choden, et al., 2023). The primary pathophysiologic mechanisms of pancreatic injury that have been identified are the direct cytopathic effects of viruses on pancreatic cells and the indirect effects through an immune-mediated response, even though these mechanisms are not fully understood (Alves, et al., 2020). We present a case study of acute pancreatitis that occurred after a mild COVID-19 infection.

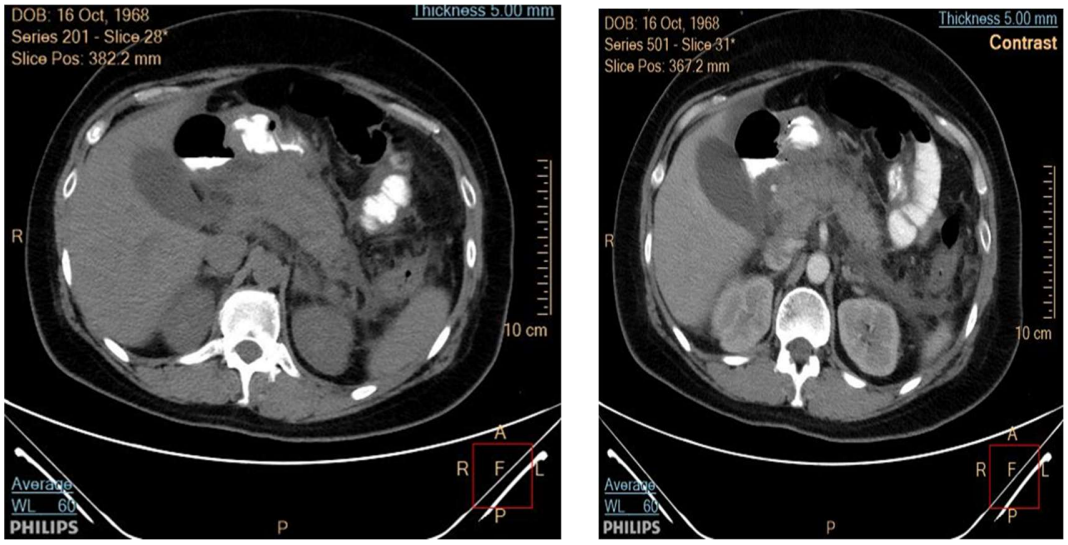
**Case Study**

A 55-year-old Caucasian female patient with an otherwise unremarkable medical history, except for a prior COVID-19 infection a year ago, presented to the emergency department with symptoms of sudden and acute epigastric pain, without any radiation, followed by multiple episodes of vomiting and diarrhoea. The symptoms started 3 hours ago. She was initially treated in a health care center with paracetamol, butylscopolamine, omeprazole, and metoclopramide without any clinical improvement. The patient mentioned the consumption of well-cooked green beans prior to the symptoms' onset. She denied any use of tobacco, herbals, or recreational drugs. She is a social drinker. Notably, the patient was unvaccinated against SARS-CoV-2. On initial assessment, the patient was alert, had a good level of consciousness, and had no focal neurological features. She was febrile and clinically stable. The physical examination of the respiratory and cardiovascular systems was unremarkable. The comprehensive abdominal exam revealed severe epigastric pain on light palpation without any clinical signs of peritoneal irritation.

The chest and abdominal X-rays were unremarkable. The ultrasound of the upper abdomen showed that it was unremarkable. The initial laboratory workups showed leukocytosis (WBCs = 23.200 x 103/µL) and inflammatory markers within the normal limits. Moreover, hypochromic microcytic anaemia [haemoglobin concentration (Hgb) of 12,60 g/L, haematocrit (Hct) level of 39,60%, mean red blood cell volume (MCV) of 64,10 fL] was found. Serum amylase was more than three times normal (AMY = 3078 IU/L). Urine amylase was highly elevated, with a value of 32.470. Fasting blood glucose and triglycerides were within normal limits. The liver enzymes and calcium levels were normal. The renal function and levels of the electrolytes were normal. Serum lipase was not measured in our laboratory due to limited facilities. Her arterial blood gases did not show any acid-base imbalances. The electrocardiogram showed sinus rhythm without any ischemic changes, and the troponin level was negative. The rapid test for SARS-COV-2 was negative.

The patient was admitted for possible acute pancreatitis in the internal medicine department. It was hypothesized that acute pancreatitis was the working diagnosis. She was immediately started on aggressive intravenous (IV) fluid resuscitation, bowel rest, and analgesics. Empiric antibiotic therapy was started with ciprofloxacin and metronidazole for possible underlying cholecystitis. Close monitoring of her vital signs and fluid balance was done. Initially, a contrast-enhanced CT scan of the abdomen was performed, which revealed diffuse enlargement of the pancreas,

heterogeneous attenuation of pancreatic parenchyma, and peripancreatic fat tissue strading, along with the presence of peripancreatic, perisplenic, and perihepatic free fluid collections. Additional imaging features were the dilation of the main pancreatic duct, common and left bile duct, as well as moderate gallbladder enlargement.




(a) (b)

**Figure 1**. Axial sections of NCECT (a) and CECT (b) show a dilated gallbladder without evidence of any calcified stone or sludge and an oedematous, mildly enlarged pancreas with stranding of the peripancreatic fat tissue. There are also small fluid collections in the hepatoduodenal ligament, around the pancreatic tail, and in the left perirenal space.

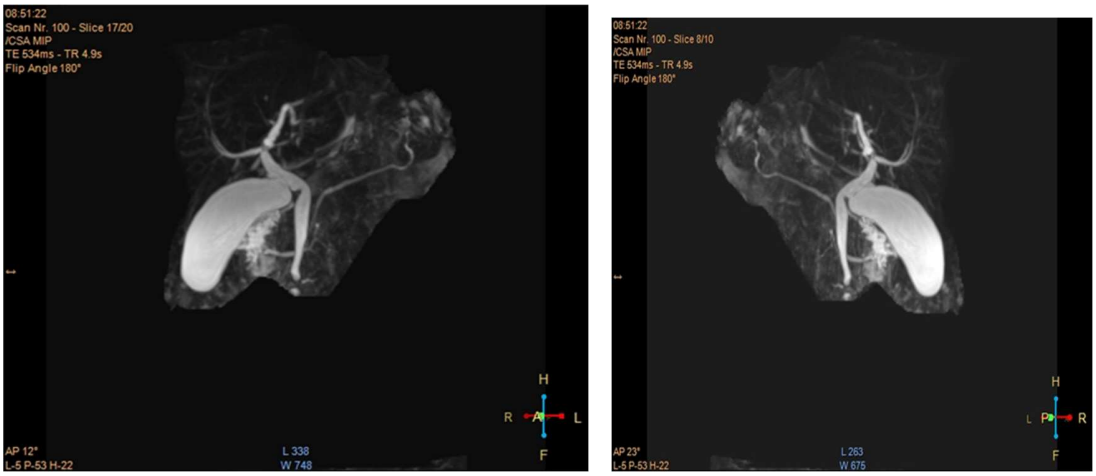



**Figure 2**. Magnetic Resonance Cholangiopancreatography reveals no filling defects within the intrahepatic or extrahepatic biliary tree. The common bile duct is slightly enlarged but tapers smoothly to the ampulla of Vater, and the pancreatic duct is mildly enlarged. There was no significant intrahepatic biliary duct dilatation. The gallbladder is distended, with no evidence of any gallstones.

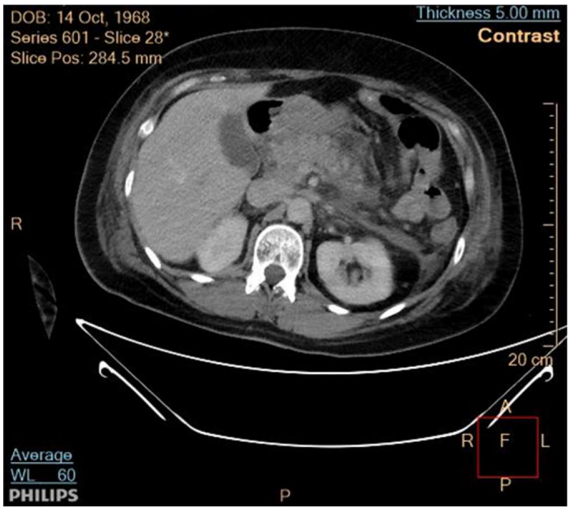



**Figure 3.** Axial section of CECT shows a mild, gradual resolution of pancreatitis. The gallbladder remains dilated, with no evidence of any gallstones. The pancreatic oedema persists, although the heterogeneity is less. The peripancreatic fat stranding and the fluid collections also persist.

Perinephric fat stranding and haziness of the right kidney were also observed. Notably, on the uppermost transverse sections of the abdominal CT scan, a small left-sided pleural effusion was accompanied by atelectasis. The imaging findings were attributed to acute pancreatitis together with extrapancreatic manifestations (Figure 1).

In the context of excluding gallstone pancreatitis, MRCP was conducted, which revealed no evidence of cholelithiasis or microlithiasis but mild dilation of the left intrahepatic bile ducts and gallbladder without thickening of its wall and mild dilation of the major pancreatic duct (Figure 2).

On the second day of her hospital stay, she complained of a dry cough. She became feverish with a body temperature of 39oC, having no other symptomatology. A repeated chest X-ray did not show any features of consolidation. The PCR test for SARS-COV-2 came back positive.

The patient was transferred to a COVID-19 isolation clinic based on national guidelines. Remdesivir was started and administered for 3 days. No supportive oxygen therapy was needed.

On the fifth day, a repeated abdominal CT scan was performed, showing a mild resolution of pancreatitis (Figure 3). Antibiotics were discontinued. Further blood tests were run to investigate the cause of the pancreatitis. Specifically, the immunological testing for IgG4-related autoimmune pancreatitis was negative. Repeated laboratory tests showed a gradual decrease in WBC count and a gradual but significant improvement in amylasemia. The rest of the laboratory findings were unchanged and unremarkable. The repeated arterial blood gases showed mild respiratory alkalosis. The blood and urine cultures were negative. Oral refeeding was reinstituted gradually as tolerated by the patient following pain alleviation, a decrease in serum amylase levels, and the presence of hunger. There was a

gradual resolution of episodes of diarrhoea. The patient was discharged after 11 days of hospitalization following symptom improvement and normal parameters in blood tests.

**Discussion**

We report a case of acute pancreatitis on the basis of an asymptomatic COVID-19 infection. Although acute pancreatitis and COVID-19 infection may be a coincidence in our case, current literature has shown that SARS-CoV-2 infection might be associated with various clinical complications involving many organ systems, except the respiratory system, like the gastrointestinal system (Cheung, et al., 2020).

ACE-2 receptors are key regulators of the metabolic pathways of the pancreas, specifically insulin secretion and glucose homeostasis (Balthazar & Chehter, 2022). Interestingly, SARS-CoV-2 is involved in the development of insulin-dependent diabetes mellitus via the destruction of pancreatic islets (Balthazar & Chehter, 2022). Literature has shown a greater expression of ACE2 receptors in the pancreatic tissue of healthy individuals as opposed to other tissues, thus strengthening the causality of pancreatic injury due to SARSCOV2 (Balthazar & Chehter, 2022). SARS-CoV-2 can lead to pancreatic injury by either directly entering the pancreatic cells through binding to ACE-2 receptors that are expressed in both the exocrine and endocrine pancreas or through a systemic and immune-mediated inflammatory response discharge (Alves, et al., 2020). Interestingly, the endocrine pancreas was found to be more susceptible in COVID-19 patients (Balthazar & Chehter, 2022). Distinct features of pancreatitis in COVID-19 infection include the typical clinical presentation of pancreatitis and metabolic dysregulation, the radiographic findings of duodenal and pancreatic inflammation along with liver steatosis, and male sex (Balthazar & Chehter, 2022).

Hyperglycemia cases have been observed as a result of the high affinity of SARSCOV2 with the ACE2 receptors in pancreatic islets, which could lead to acute diabetes. Recent data revealed that a small percentage of patients will develop diabetes three years following hospital discharge (Alves, et al., 2020). A mounting number of published studies revealed the development of acute pancreatitis during or following the COVID-19 infection (EBiK, et al., 2022). In a cohort study by Inamdar et al., idiopathic pancreatitis was found to be the most frequent form of pancreatitis in patients with COVID-19 infection. (Balthazar & Cheter, 2022) Drug-induced pancreatitis has been observed in COVID-19 patients following treatment with antiviral agents like lopinavir/ritonavir, tocilizumab, and antipyretics (Balthazar & Chehter, 2022).

The diagnosis of pancreatitis is based on clinical manifestations, laboratory tests and radiographical studies (Kataria, et al., 2020). According to the revised diagnostic criteria of the Atlanta Classification, for the diagnosis of pancreatitis, two of the following three criteria should be met: 1) characteristic epigastric abdominal pain characterized by sudden onset and radiation to the back; 2) increased levels of serum amylase or lipase three times the upper limit of normal; and 3) typical radiographic findings (contrast-enhanced computed tomography (CECT), MRI, and ultrasonography (Choden, et al., 2023). The two common aetiologies of pancreatitis are gallstones and alcohol consumption. Other established risk factors include medications, hypertriglyceridemia, and hypercalcemia (Cheung, et al., 2020).

Apart from these, viruses are also considered causative agents of pancreatitis, with the most prevalent viruses being hepatitis A and B,

coxsackie, mumps, Epstein-Barr virus, and measles (Cheung, et al., 2020). Approximately infectious agents have been implicated in 10% of acute pancreatitis cases. Since the beginning of the COVID-19 pandemic, a few cases of COVID-19-related acute pancreatitis presented with various symptomatologies and diagnosed as AP in different stages of their hospitalisation have been reported (Lakshmanan & Mali. 2020).

According to Ranson's criteria, severe pancreatitis was unlikely. Our patient had an unremarkable medical history. The imaging studies ruled out any obstructive causes of pancreatitis. There was not any clinical evidence of viral infection caused by cytomegalovirus, measles, coxsackie mumps, Epstein-Barr virus, varicella zoster virus, or herpes simplex virus. The result of her serological test for hepatitis B and C viruses was negative. Hyperglycemia did not develop during her hospital stay. Food-induced pancreatitis was excluded due to the lack of allergic symptomatology and elevated IgE levels in blood tests (Manohar, et al., 2017).

Eosinophilic pancreatitis was also excluded due to the absence of gastrointestinal manifestations like mucosa thickening and normal eosinophil levels in blood tests. Additionally, cases of acute pancreatitis have been reported following the consumption of either improperly prepared or raw green beans. Based on recent data, a substance known as phytohemagglutinin that is found in toxic doses in undercooked or raw green beans can induce the secretion of cholecystokinin and lead to acute pancreatitis (Niederau, C., & Grendell, 1999). However, in our case, the beans were well cooked.

In our case, after ruling out the commonest risk factors of pancreatitis, we conclude that SARS-CoV-2 was the etiological factor of acute pancreatitis. Thus, infection of SARS-COV-2 should be included in the differential diagnosis of patients with pancreatitis, following the exclusion of other most frequent causes. Moreover, during the COVID-19 infection, great focus should be placed on both clinical and radiographical findings for the early identification of these two diseases. Early diagnosis is of paramount importance for sufficient treatment and optimum management of systemic manifestations like systemic inflammatory response syndrome.

**Conclusion:** The current data available are still controversial concerning the implication of pancreas in patients with COVID-19 infection, as various confounding factors are involved in the diagnosis of acute pancreatitis during COVID-19 infection. SARS-CoV-2 should be included in the differential diagnosis of acute pancreatitis. Attention should be paid to the timely diagnosis and management of patients with acute pancreatitis and the COVID-19 infection to prevent any complications that could increase the risk of morbidity and mortality. Additionally, SARSCoV-2 transmission can be prevented among healthcare workers and caregivers by following precautionary measures.

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