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Acute pancreatitis following SARS-CoV-2 infection: A case report

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Abstract

The novel coronavirus 2019 (COVID-19) which is caused by severe acute respiratory syndrome coronavirus-2 was first reported from Wuhan, China in December 2019. Since then, it has caused global crisis and it still continues to be a Public Health Emergency of International Concern. Although it primarily involves respiratory system with symptoms ranging from mild to severe acute respiratory distress syndrome, extrapulmonary involvement including gastrointestinal manifestations is increasingly reported. There are few reported cases of acute pancreatitis following severe acute respiratory syndrome coronavirus-2 infection; however, little is known on true prevalence of acute pancreatitis or other extrapulmonary manifestations. More data and research on pathophysiology and organ-specific extrapulmonary manifestations would aid clinicians to monitor and recognise these wide spectra of manifestations so that organ-specific therapeutic strategies and management pathways could be developed. We report a case of acute pancreatitis in an otherwise asymptomatic severe acute respiratory syndrome coronavirus-2 infection. He developed acute upper abdominal pain on day 13th of severe acute respiratory syndrome coronavirus-2 infection detection. Diagnosis of acute pancreatitis was made after his serum amylase level was raised by more than five times the normal and the computed tomography abdomen showed oedematous pancreas. He was successfully managed and discharged after 12 days of diagnosis of acute pancreatitis. On follow-up after 1 year, there were no recurrent attacks of pancreatitis. Our case highlights that acute pancreatitis can occur even in asymptomatic and milder form of COVID-19 and the onset of such complications could be delayed. Abdominal pain in COVID-19 should be carefully assessed because prompt diagnosis and management of acute pancreatitis in COVID-19 patient is crucial in preventing multi-organ dysfunction leading to subsequent morbidity and mortality.

Keywords

Acute pancreatitis, acute respiratory distress syndrome, COVID-19, computed tomogaphy scan abdomen, pneumonia, severe acute respiratory syndrome coronavirus-2

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Introduction

The coronavirus 2019 (COVID-19) pandemic resulted in over 756 million confirmed cases and over 6.8 million deaths globally since the start of pandemic. More than 6.7 million new cases and over 64,000 deaths were reported within a period of last 1 month as of 15 February 2023.[1] Since the start of the pandemic, every aspect of our lives has been affected in last 3 years. It has caused major economic and social disruption with frequent lockdowns and closing of international borders leading to increase in poverty and food insecurity particularly among vulnerable groups. Furthermore, major disruption to the delivery of essential health services such as routine childhood immunisations, antenatal care and non-communicable diseases has led to additional loss of human lives. These devastating effects were particularly felt in poor low-income countries. With ongoing new mutations and significant new infections, the World Health Organization (WHO) still considers

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COVID-19 as a threat to public health. Although it is mainly considered to be an infection of the respiratory tract with clinical spectrum ranging from asymptomatic to severe pneumonia[2] and acute respiratory disease syndrome (ARDS), extrapulmonary manifestations including gastrointestinal symptoms are not uncommon.[2–4] Some of the important and deleterious extrapulmonary manifestations of COVID-19 include stroke, encephalopathy, Guillain–Barré syndrome, thromboembolism, myocarditis, arrhythmias, acute coronary syndromes, hyperglycaemia, ketosis, gastrointestinal symptoms and acute kidney injuries. The possible underlying pathophysiology for these multiple organ injuries following severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection includes direct viral toxicity of cells and tissues through angiotensin-converting enzyme 2 (ACE 2) receptor–mediated viral entry into host cells, endothelial cell dysfunction, dysregulated immune response and dysregulated renin–angiotensin–aldosterone system.[5] Rarely pancreatitis can be one of the extrapulmonary complications of COVID-19 as reported earlier from few centres in other countries. The clinical spectrum of pancreatic involvement in COVID-19 can range from asymptomatic abnormal pancreatic enzyme elevation[6] to acute pancreatitis (AP). Although most reported cases of AP in COVID-19 had accompanying respiratory symptoms or fever, AP can rarely be an initial presentation of COVID-19 or an isolated symptomology without other features of COVID-19.[7] We report a case of AP in a young male with an otherwise asymptomatic SARS-CoV-2 infection.

Case report

A 25-year-male, clinically asymptomatic, was tested positive for SARS-CoV-2 by real-time reverse transcription polymerase chain reaction (PCR) in a nasopharyngeal swab sample on 29 June 2021 during contact tracing. We did not do genomic sequencing for virus mutation in our patient but the virus variant circulating in the community and the neighbouring countries at that time was Delta variant (B.1.617.2). He was subsequently admitted in COVID-19 isolation facility as per the national guideline,[8] which required every positive case to be isolated for at least 21 days in a designated isolation facility.

On 13th day of isolation, he developed sudden onset of severe epigastric pain radiating to the scapula and back. It was associated with nausea, vomiting and anorexia. He did not have fever and respiratory symptoms like cough or shortness of breath. His bowel habits were normal prior to the onset of abdominal pain but subsequently developed constipation. He did not reveal any similar episodes in the past and not known to have other co-morbid illnesses including peptic ulcer, gallstone and autoimmune diseases. He was a social drinker and did not smoke or use any form of medicines or other substances.

Initial physical examination showed tachycardia (Heart Rate 125/min), blood pressure of 138/92 mm Hg, respiratory rate of 24/min with oxygen saturation (SaO_2) of 98 % in room air and normal temperature. Abdomen was soft with mild tenderness in the epigastric region.

Laboratory investigations revealed raised serum amylase with value of more than three times normal (1331 IU/L), neutrophilic leucocytosis and lymphopenia, raised transaminases (Aspartate aminotransferase [AST] of 80 IU/L, Alanine aminotransferase [ALT] of 57 IU/L), mild hypocalcaemia, raised C-reactive protein (CRP) (13.2 mg/dL) and serum ferritin (1092 ng/mL). Fasting blood sugar and triglycerides were within normal limits (Table 1). Serum lipase, IL-6, D-dimer, Fibrin degradation products (FDP) were not done in our laboratory due to lack of facilities. Serology for HIV, hepatitis B and C virus was negative.

Chest X-ray (Figure 1) was unremarkable and X-ray abdomen (Figure 2) showed only focal dilatation of distal and transverse colon. Computed tomography (CT) scan of abdomen (Figures 3 and 4) revealed swollen and oedematous body and tail of pancreas with mild peripancreatic fat stranding. Multiple rim-enhancing collections were noted in the peripancreatic region. No evidence of cholelithiasis or microlithiasis and necrosis were noted. Modified CT severity index was 6 suggesting moderate pancreatitis.

He was managed conservatively with bowel rest, IV fluids and analgesics. Close monitoring of his vital parameters including fluid balance was done. On day 3 of the onset of pancreatitis, the patient continued to have persistent tachycardia (146/min), drop in blood pressure (98/68 mm Hg) with desaturation (SPO_2 85%–91%) and reduced urine output amounting to oliguria (10 mL/h for more than 12 h). In addition to maintenance IV fluids, low-dose vasopressor support with noradrenaline was started to achieve target blood pressure. His oxygen saturation was achieved with minimal flow rate of oxygen supplementation. He started having adequate urine output after 24 h of vasopressor support and fluid resuscitation and did not require vasopressor support and oxygen supplementation after 48 h. Oral intake was resumed gradually as tolerated by patient after subsiding the pain and bowel opening.

On improvement of symptoms and clinical parameters, the patient was discharged on 22 July 2021 (23 days after testing positive for COVID-19 and 12 days after developing AP). On follow-up after 1 year, the patient is doing well with no recurrent attacks of pancreatitis.

Discussion

We described a case of AP in an asymptomatic SARS-CoV-2 infection in this study. According to the revised Atlanta classification and definition, the diagnosis of AP requires two of the following three features: (1) abdominal pain consistent with AP, (2) serum lipase activity or amylase activity at least three times greater than the upper limit of normal and (3) characteristic findings of AP on abdominal imaging studies

Table 1. Summary of laboratory investigation reports of the patient.

Laboratory investigations	Initial test results (11 July 2021)	Repeat tests results (17 July 2021)	Repeat test results (21 July 2021)	Reference range
Complete blood count				
White cell count $\times 10^3/\mu L$	25.7	17.4	13.1	4.0–10.0
Lymphocyte (%)	5	10	18	20–40
Neutrophil (%)	88	77	68	40–60
Haemoglobin (g/dL	16.3	12.6	12.2	14.0–18.4
Haematocrit (%	49	37	39	39–50
Platelet $\times 10^3/\mu L$	340	355	380	150–450
Liver function test				
AST (IU/L)	80	45		0–35
ALT (IU/L)	57	36		0–45
Alkaline phosphate (IU/L	122	146		74–237
Total bilirubin (mg/dL)	1.8	1.5		0.2–1.0
Direct bilirubin (mg/dL)	0.4	0.4		0.0–0.2
Albumin (g/dL)	3.2			3.5–5.0
Renal function test				
Urea (mg/dL)	34	26		15 – 45
Creatinine (mg/dL)	1.2	0.7		0.6–1.3
Serum amylase (IU/L)	1331			0.0–260
Inflammatory markers				
Serum ferritin (ng/mL)	1092			20–300
C-reactive protein (mg/dL)	13.2	9.7	3.3	0.0–0.6
LDH (IU/L)	944			180–325
Electrolytes				
Sodium (mEq/L)	136			135–145
Potassium (mEq/L)	4.7			3.6–5.0
Calcium (mg/dL)	7.7	8.7		8.4–10.2
Magnesium (mg/dL)	1.8			1.8–2.6
Lipids and blood sugar				
Total cholesterol (mg/dL)	116			$<$200
Triglycerides (mg/dL)	76			0.0–150
Fasting blood sugar (mg/dL)	78		90	70–100

AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; LDH: lactate dehydrogenase; IU/L: International Units per Liter.

(Contrast-enhanced computed tomography (CECT) and less commonly Magnetic resonance imaging (MRI) or ultrasonography). Severity can then be graded as mild (no organ failure and no local or systemic complications), moderately severe (transient organ failure that resolves within 48 h and/or local or systemic complications without persistent organ failure) and severe (persistent single or multiple organ failure lasting $>$48 h).[9]

Our patient was classified as having moderately severe form of AP since he had features of transient organ failure and local complications. We ruled out common aetiologies of AP through history and relevant investigations. Although the patient gave history of consuming alcohol during gatherings, he had not consumed any alcohol-related drinks for more than a month since he was in a quarantine facility followed by admission in COVID-19 isolation facility. There was no evidence of cholelithiasis or microlithiasis in the abdominal imaging.

Infections by certain viruses such as cytomegalovirus, Epstein-Barr virus, hepatitis viruses, measles, mumps, HIV, varicella zoster-virus, coxsackie and herpes simplex virus have been implicated in the aetiology of AP;[10,11] however, there were no clinical features indicating these viral aetiologies in our patient. His serological tests for HIV, Hepatitis B and C viruses were negative. The temporal relation between SARS-CoV-2 infection and the onset of AP with lack of evidence of other common aetiologies suggest coronavirus-induced pancreatitis in our patient.

SARS-CoV-2 virus enters host cells by binding of its spike proteins to angiotensin-converting enzyme 2 (ACE2) receptor and subsequently gets activated by human proteases.[12] It was found that ACE2 receptors are expressed in both exocrine glands and islets of pancreas in normal people with slightly higher proportion in pancreas than in the lungs.[13] This finding indicates that SARS-CoV-2 can also bind to ACE 2 receptors expressed in pancreas which can

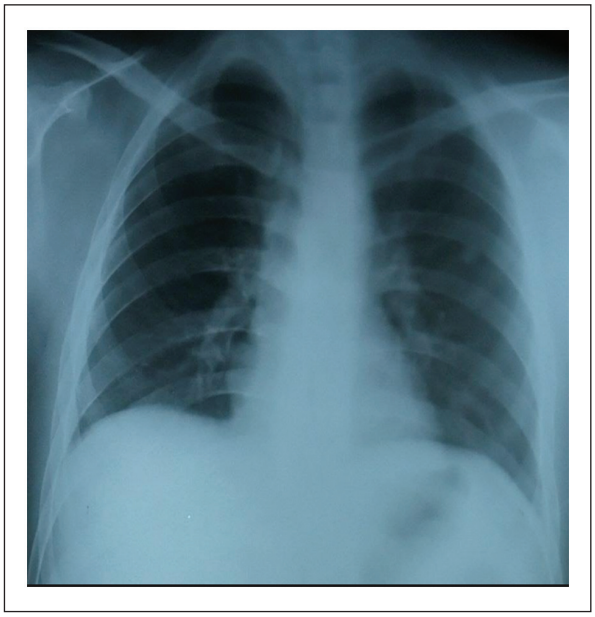

Figure 1. Normal chest X-ray PA view.

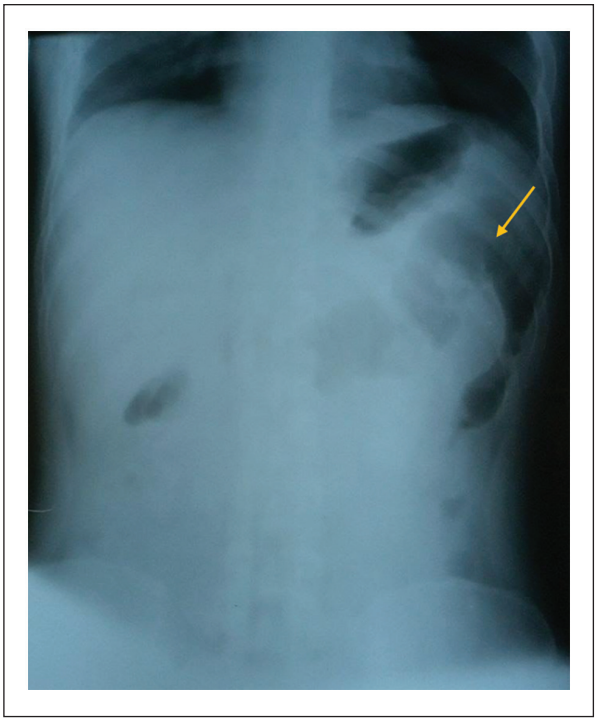

Figure 2. X-ray abdomen (erect PA view) showing focal dilatation of transverse and distal colon (yellow arrow).

lead to pancreatic injury. The pancreatic injury could be due to direct cytopathic effect of SARS-CoV-2 virus on pancreatic cells as supported by detection of SARS-CoV-2 RNA in pancreatic fluid collection by Schepis et al.[14] Pancreatic cells can be also injured indirectly as a result of systemic immunological response to SARS-CoV-2

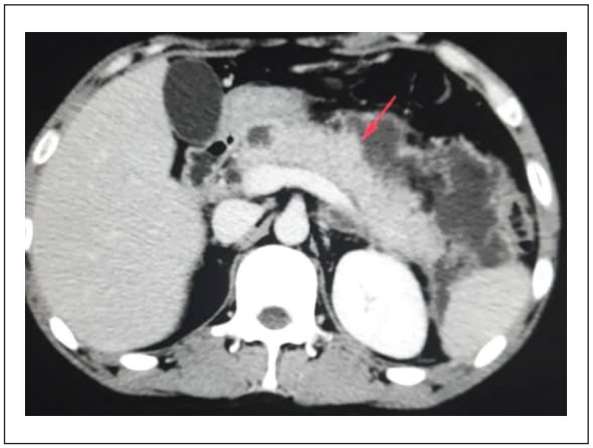

Figure 3. Contrast enhanced CT of the abdomen axial scan at the level of L1 vertebra showing oedematous and swollen body of pancreas (red arrow).

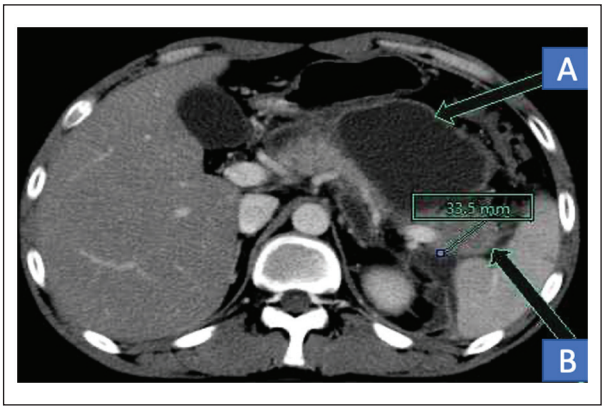

Figure 4. Contrast-enhanced CT of the abdomen axial scan at the level of T12 vertebra showing large walled-off collection (arrow A) in the peripancreatic region involving lesser sac and swollen tail of pancreas (arrow B).

infection as simultaneous multiple organ injuries such as liver, heart and kidneys have been documented in patients with COVID-19 pneumonia and pancreatic injury.[6] Our patient had raised inflammatory markers such as serum ferritin, CRP and lactate dehydrogenase (LDH) with neutrophilic leucocytosis and lymphopenia indicating possible hematologic and immune system mediated manifestation of COVID-19.[5,15]

The incidence of pancreatic injury (defined by any abnormalities in lipase or amylase) by SARS-CoV-2 infection without clinical features of AP has been reported as high as 17% in a case series of 52 patients with COVID-19 pneumonia.[6] A retrospective study in America reported a point prevalence of AP of 0.27% among patients hospitalised with COVID-19.[16] A meta-analysis from China, USA and European countries found pooled prevalence of AP to be 3.1% among patients with COVID-19.[17] However, the true prevalence of AP in COVID-19 is not known.

Our patient did not have any respiratory symptoms or other clinical manifestations of COVID-19 when he developed AP. Few similar cases were reported from other countries with AP as presenting symptoms of COVID-19 without accompanying fever or respiratory symptoms,[7,18] while in majority of the cases AP followed the initial respiratory symptoms or COVID-19 pneumonia.[19–24] It may be worthwhile to consider SARS-CoV-2 infection as possible viral aetiology for AP in patients without apparent cause even in absence of fever or respiratory symptoms.

The onset of pancreatitis in our patient was almost 2 weeks after detection of SARS-CoV-2 infection by RT-PCR which is comparable to previous reported cases from other countries.[24,25] Around the time of onset of pancreatitis, only the antibodies against SARS-CoV-2 was positive, and the repeat RT-PCR was negative since it was already 2 weeks following the infection. These findings in our case point towards the possible indirect injury to pancreas during dysregulated systemic immunological response to SARS-CoV-2 infection.

Conclusion

This case highlights that COVID-19 can involve multiple organs and AP can be a presenting symptom even without concurrent respiratory symptoms. Abdominal pain in COVID-19 patient must be carefully evaluated and AP should be kept high in the list of differentials. Prompt diagnosis of AP in a patient with COVID-19 is essential for early initiation of appropriate management in order to prevent further complications. Delays in early recognition and treatment of such complications would lead to irreversible multiple organ failure leading to significant morbidity and mortality.

In view of COVID-19 being still considered as a threat to public health with ongoing new infections and deaths related to COVID-19 worldwide, it is important to consider SARS-CoV-2 infection as a possible aetiology in a patient presenting with AP with no other apparent cause. This would not only help appropriate management of patient to prevent further morbidity and mortality but also would help health workers and caregivers to take precautionary measures to prevent further transmission of virus during patient care.

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Author contributions

UC: conception, literature review, manuscript preparation, critical revision, photography and final approval.
SY: manuscript preparation, literature review design, critical revision and final approval.
GP: manuscript preparation, literature review, critical revision and photography.
PW: manuscript preparation, literature review and critical revision.

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Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed consent

Written informed consent was obtained from the patient(s) for their anonymised information to be published in this article.

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