

# Acute pancreatitis in a patient with COVID-19

Rawan A Rahman AlHarmi <sup>1</sup>, Tahera Fateel,<sup>1</sup> Jalila Sayed Adnan,<sup>2</sup> Kamel AlAwadhi<sup>1</sup>

<sup>1</sup>Department of Surgery,  
Salmaniya Medical Complex,  
Manama, Bahrain

<sup>2</sup>Department of Radiology,  
Salmaniya Medical Complex,  
Manama, Bahrain

## Correspondence to

Dr Rawan A Rahman AlHarmi;  
rawan.alhermi@gmail.com

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## SUMMARY

COVID-19 mainly causes pulmonary disease. Involvement of gastrointestinal and hepatobiliary systems, among other systems, has been reported. We report a case of acute pancreatitis in a patient with resolving COVID-19 pneumonia. History taking and investigations excluded other causes of pancreatitis. This case demonstrates the possibility of pancreatic injury in patients with COVID-19, in line with previously reported similar cases. We believe that it is imperative to screen patients presenting with acute pancreatitis for SARS-CoV-2. It is also important to take into consideration that patients with a complicated course who require an invasive procedure such as drainage might pose a risk of transmission to the operating surgeon or interventionist.

## BACKGROUND

COVID-19, caused by SARS-CoV-2, mainly causes pulmonary disease. It emerged and was first identified in Wuhan, China in hospitalised patients with pneumonia of unknown origin between December 2019 and January 2020. However, extrapulmonary manifestations affecting gastrointestinal and hepatobiliary systems, among other systems, have been reported. Patients can present with symptoms including anorexia, nausea and/or vomiting, diarrhoea and abdominal pain.<sup>1 2</sup> We report a case of acute pancreatitis in a patient with COVID-19 pneumonia without any other known causes.

## CASE PRESENTATION

This patient is a 52-year-old woman with a medical history of type 2 diabetes mellitus, hypertension, hypothyroidism and morbid obesity. The patient developed symptoms of fever, dry cough and shortness of breath over a duration of 1 week and tested positive for SARS-CoV-2 through a nasopharyngeal swab, detected by real-time reverse transcription PCR, with a cycle threshold value of 24. The patient denied abdominal pain on initial presentation. Contact with a positive case was reported. The patient was admitted to an isolation facility as per national protocols for mildly symptomatic patients who are not eligible for home isolation.<sup>3</sup>

On the sixth day, she developed worsening of cough and shortness of breath with hypoxia and was hence transferred to a treatment facility designated for cases with moderate pneumonia. Chest radiograph showed bilateral infiltrates and so she was treated as COVID-19 pneumonia as per protocol (figure 1A–C).<sup>3</sup> The patient was started on a steroid course for a total of 15 days (including dexamethasone and methylprednisolone), ceftriaxone, doxycycline, azithromycin, enoxaparin, vitamin D, zinc, fluticasone furoate/vilanterol,

salbutamol, ipratropium bromide, pantoprazole, omeprazole, metoclopramide and paracetamol, in addition to her regular home medications (table 1). Prone and incentive spirometry were employed as well. The patient required oxygen through nasal cannula and face mask.

As the pneumonia was resolving and the patient was being prepared to be discharged, she developed abdominal pain. At that time, she had already tested negative for SARS-CoV-2 on two nasopharyngeal swabs obtained as exit swabs on days 17 and 18 from the initial swab. CT scan of the abdomen was done and showed an atrophic pancreas with diffuse fatty infiltration, minimal peripancreatic fat stranding and fluid, and reactive lymph nodes. The imaging findings were suggestive of early acute pancreatitis without necrosis, pseudocyst nor gas formation (figure 2). COVID-19 pneumonia changes were evident in the lower cuts of the chest in the form of bilateral ground-glass consolidation, mainly peripherally (figure 3A–C).

General surgery consultation was sought. On obtaining further history, the patient reported that the pain has been present for at least 1 week, treated initially as gastritis. However, it was gradually increasing in severity. The pain was mainly epigastric and affecting the right upper quadrant, burning in nature, often radiating to the back and was aggravated by oral intake. It was accompanied by nausea and vomiting. The patient denied any previous similar episodes. She also denied alcohol intake. Her surgical history was significant for a laparoscopic cholecystectomy performed 10 years earlier for gallstone disease and a hysterectomy 5 months earlier for uterine fibroids.

## INVESTIGATIONS

Laboratory investigations done on consulting general surgery are summarised in table 2 including those done to rule out the causes of acute pancreatitis. Liver function tests revealed a mild increase in gamma-glutamyl transferase (GGT) and alanine aminotransferase and were otherwise within normal limits. Lipase is not available in our laboratory and hence was not done. Inflammatory markers were generally improving.

## DIFFERENTIAL DIAGNOSIS

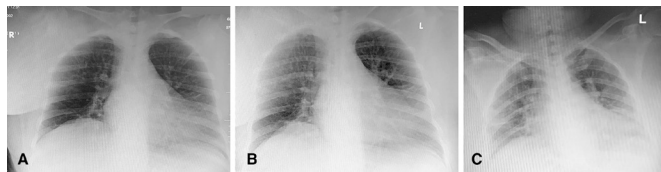
Initially, we thought that pancreatitis was caused by hypertriglyceridaemia; however, lipid profile was repeated and triglyceride level was almost normal. The patient did not undergo any invasive procedure, namely endoscopic retrograde cholangiopancreatography nor recent surgery. No previous similar episodes to suggest chronic nature or genetic predisposition were reported. No recent trauma, exposure to envenomation nor ischaemic



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**Figure 1** (A–C) Chest radiographs of the patient on days 1, 3 and 6 of the disease.

insult was reported. Anatomical pancreatic anomalies were not evident on imaging studies. Personal history was negative for pancreatic cancer. Moreover, during her hospital course, our patient received multiple drugs that have been associated with pancreatitis, so drug-induced acute pancreatitis is possible (table 1). Nevertheless, with a multitude of cases published of patients with COVID-19 developing pancreatitis, an association is possible.

### TREATMENT

The patient was transferred to a regular surgical ward for further management. From a surgical point of view, she was started on conservative management including intravenous fluids and bowel rest. Oral intake was resumed gradually as tolerated. The patient was maintaining adequate oxygen saturation on room air. However, her pain was not improving and a repeated abdominal CT was done around a week later. It showed a localised fluid density at the level of the body of the pancreas anteriorly, measuring 3.1×1.5 cm, which was faintly present on the prior scan. On improvement of pain, the patient was discharged home.

**Table 1** Summary of received medications

Medication	Dose and route of administration	Duration
Dexamethasone	6 mg intravenously once daily	2 days
Methylprednisolone	40–60 mg intravenously every 8 hours	8 days
Dexamethasone (following discontinuation of methylprednisolone)	6 mg per oral once daily	5 days
Ceftriaxone	2000 mg intravenously once daily	8 days
Doxycycline	100 mg per oral two times per day	2 days
Azithromycin	500 mg per oral once daily	5 days
Enoxaparin	4000–12 000 IU subcutaneously two times per day	Throughout hospital stay
Cholecalciferol	50 000 IU per oral once weekly	
Zinc gluconate	50 mg per oral once daily	
Fluticasone furoate/vilanterol	1 puff once daily	From second day of admission onwards
Nebulised salbutamol	5 mg every 8 hours	
Nebulised ipratropium bromide	250 µg every 8 hours	
Pantoprazole	20 mg per oral once daily	According to permit of oral intake and drug availability
Omeprazole	20 mg intravenously two times per day/20 mg per oral two times per day	
Metoclopramide	10 mg intravenously every 4 hours as needed	Limited use
Paracetamol	1000 mg per oral or intravenously every 6 hours as needed	

µg, micrograms; IU, international units; mg, milligrams.



**Figure 2** Axial cuts of intravenous contrast-enhanced CT of the abdomen at the level of the pancreas. Mild fatty infiltration of the pancreatic parenchyma is noted with mild diffuse peripancreatic fat stranding and focal single small volume fluid collection anterior to the neck of the pancreas (arrow). No necrosis, calcification or haemorrhage. According to Balthazar score, the CT severity index is 3. This score is consistent with mild acute pancreatitis.

### OUTCOME AND FOLLOW-UP

The patient stayed for a total of 23 days in the hospital, of which 9 days were under the care of general surgery. The patient was seen in the general surgery outpatient clinic 10 days following discharge on a follow-up visit and was doing well.

### 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>4</sup>

Several viruses have been implicated in the aetiology of acute pancreatitis. These include 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.<sup>5</sup>

COVID-19 is caused by SARS-CoV-2. SARS-CoV-2 enters the host cells via its spike (S) protein which binds to angiotensin-converting enzyme 2 (ACE2). In the initial phase of the disease, infection of the upper respiratory tract ACE2-expressing nasal epithelial cells occurs in asymptomatic individuals. Later in the disease course, infection of lower respiratory tract ACE2-expressing cells causes pneumonia.<sup>6</sup> The virus mainly causes pulmonary disease; however, extrapulmonary manifestations affecting gastrointestinal and hepatobiliary systems, among other systems, have been reported. Pathophysiology is likely multifactorial. Mechanisms suggested include direct tissue damage, inflammation-mediated damage and microvascular



**Figure 3** (A) Chest CT scan (lung window) showing bilateral peripheral areas of ground-glass opacity, changes during the peak stage of known COVID-19 infection. (B,C) Chest CT scan (lung window) showing massive consolidation in the posterior parts of the lower lung lobes, changes of peak stage of known COVID-19 infection.

**Table 2** Summary of laboratory investigations

Laboratory investigation	Results	Laboratory reference range
White cell count, $\times 10^9/L$	19	3.9–9.6
Serum amylase, U/L	47	30–118
Urinary amylase, U/L	219	<650
Arterial blood gas on room air		
pH	7.472	7.35–7.45
Partial pressure of carbon dioxide, mm Hg	34.9	35–45
Partial pressure of oxygen, mm Hg	70.8	80–100
Oxygen saturation, %	95.3	95–100
Bicarbonate ( $HCO_3^-$ ), mmol/L	26.3	22–28
Lactic acid, mmol/L	2.9	0.2–1.8
Calcium, mmol/L	2.38	2.15–2.50
Total bilirubin, $\mu\text{mol/L}$	4	5–21
Gamma-glutamyl transferase, U/L	102	5–55
Alanine aminotransferase, U/L	37	<33
Triglyceride (initial), mmol/L	3.4	0.2–1.8
Triglyceride (1 day later), mmol/L	1.9	
Parathyroid hormone, pmol/L	7.5	1.96–9.33
IgG, g/L	9.27	5.4–16.5
C reactive protein, mg/L	1.09	0–3

injury as observed in the small bowel.<sup>1</sup> Moreover, in a study by Liu *et al*,<sup>7</sup> expression of ACE2 in normal pancreases was found to be slightly higher than that of the lungs and it was expressed in both the exocrine glands and islets of the pancreas. The study shed light on the possibility of pancreatic injury in patients with COVID-19, based on the above findings and on a cohort of patients with non-severe and severe disease who exhibited features of pancreatic involvement.<sup>7</sup> Additionally, Schepis *et al*<sup>8</sup> reported the detection of SARS-CoV-2 RNA in a fluid sample obtained from a pancreatic pseudocyst in a patient with COVID-19 pneumonia and acute pancreatitis.

Several cases of pancreatitis in patients with COVID-19 were reported. Gonzalo-Voltas *et al*<sup>9</sup> reported a case of pancreatitis from Spain in the absence of the most common risk factors: alcohol and gallstones.<sup>9</sup> Lakshmanan and Malik<sup>10</sup> 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. Moreover, Brikman *et al*<sup>11</sup> reported a case of a patient with COVID-19 pneumonia who developed acute pancreatitis 14 days following admission. The patient did not have any history of pancreatitis, gallstones nor alcohol intake.<sup>11</sup> Further supportive data are provided by Meireles *et al*<sup>12</sup> 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>12</sup> Additional similar cases were reported by Aloysius *et al*,<sup>13</sup> Kataria *et al*,<sup>14</sup> Mazrouei *et al*,<sup>15</sup> Karimzadeh *et al*,<sup>16</sup> Hadi *et al*,<sup>17</sup> Kumaran *et al*<sup>18</sup> and Wang *et al*.<sup>19</sup>

Reports from Wuhan, China provide great insight into this possible association. Among 52 patients with COVID-19 pneumonia, 9 (17%) were found to have pancreatic injury. Patients with pancreatic injury were noted to have a more severe illness on admission. They were more likely to have loss of appetite and diarrhoea. With regard to laboratory values, they were noted to have higher levels of aspartate aminotransferase, GGT, creatinine, lactate dehydrogenase and erythrocyte sedimentation rate.<sup>20</sup> Interesting findings are provided by Szatmary *et al*<sup>21</sup> on

the characteristics of patients with COVID-19 and pancreatitis. They suggest that a combination of male sex, abdominal pain, pancreaticoduodenal inflammation with steatosis on imaging and metabolic stress (indicated by elevation of glucose and triglyceride) represents a distinct subset of patients in whom the endocrine pancreas is particularly vulnerable.<sup>21</sup> Moreover, a paediatric case has also been reported. The child presented with multisystem inflammatory syndrome, with acute pancreatitis being the initial manifestation of this syndrome.<sup>22</sup>

During her hospital course, our patient received multiple drugs that have been associated with pancreatitis (table 1). These include dexamethasone, omeprazole, paracetamol, ceftriaxone and doxycycline. Accordingly, drug-induced pancreatitis can still be considered.<sup>23</sup>

Linking acute pancreatitis to COVID-19 requires further investigation to establish an association. Acute pancreatitis is a common disease and can often be idiopathic with no identifiable aetiology. Besides, many patients with COVID-19 who are considered contagious might have not been investigated thoroughly with tests such as endoscopic ultrasonography so some causes might have been missed. It should also be taken into consideration that many reported cases have had heterogenous results, making it difficult to draw conclusions. Nevertheless, pancreatitis seems to be an uncommon complication of COVID-19.<sup>24</sup> A study from the USA revealed a point prevalence of 0.27% of acute pancreatitis in hospitalised patients with COVID-19.<sup>25</sup> Another study from Spain reported a frequency of 0.07%.<sup>26</sup> Further studies are needed to evaluate the incidence compared with that of pre-COVID-19 times.<sup>24</sup>

What does this mean to us as surgeons? The pancreas can be involved in COVID-19 infection. 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 an invasive procedure such as drainage might pose a risk of transmission to the operating surgeon or interventionist so precautionary measures must be taken.<sup>27</sup>

To sum up, in our patient, routine investigations were carried out to determine the cause of pancreatitis and many causes were ruled out. Although causality cannot be established through this case report only, we believe that COVID-19-induced pancreatitis is still to be considered, in line with the above case reports. Further data are required to determine the impact of this virus on the pancreas and the underlying pathophysiology.

### Learning points

- ▶ Several viruses have been implicated in the aetiology of acute pancreatitis.
- ▶ The exact mechanism by which viruses cause pancreatitis is unknown.
- ▶ The pancreas can be involved in COVID-19 infection.
- ▶ It is imperative to screen patients presenting with acute pancreatitis for SARS-CoV-2.
- ▶ Further studies are required to determine the association between pancreatitis and COVID-19.

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#### ORCID iD

Rawan A Rahman AlHarmi <http://orcid.org/0000-0002-7097-261X>

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