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BRIEF REPORT

Acute Pancreatitis as the Initial Manifestation in 2 Cases of COVID-19 in Wuhan, China

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Clinical data on coronavirus disease 2019 (COVID-19) with pancreatic injury are extremely limited. An acute manifestation of acute pancreatitis in COVID-19 has not been reported. We describe here 2 cases of COVID-19 with acute pancreatitis as the initial manifestation in Wuhan, China. Patient 1 died despite maximal mechanical ventilatory support and circulation support, while patient 2 was finally discharged after showing significant improvement. Low T cells in peripheral blood may indicate a poor outcome.

Keyword. acute pancreatitis; COVID-19; initial manifestation; Wuhan.

An outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that began in Wuhan, Hubei Province, China, has spread rapidly to multiple countries, causing a public health crisis [1, 2]. Many studies have confirmed that SARS-CoV-2 infections can cause multiple organ damage. The lungs, heart, kidneys, immune system, and coagulation system are common targets of SARS-CoV-2 [3, 4]. It has been reported that COVID-19 can be combined with pancreatic injury [5, 6]. Recently, some reports of COVID-19-associated acute pancreatitis have been published in the literature [7, 8]. However, onset of acute pancreatitis in COVID-19 patients has not been reported. We describe 2 cases of COVID-19 with acute pancreatitis as the initial manifestation.

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CASE PRESENTATION

Case 1

A 42-year-old male was admitted on February 28, 2020, with a history of nausea and persistent upper abdominal pain with radiation to the back for 3 days. He did not complain of fever, cough, fatigue, or diarrhea. He denied drinking, taking medicine, or overeating in recent days. He had no history of gallstone or autoimmune disease. Abdomen computed tomography (CT) on February 28 (day 3 of illness) revealed prominence of the pancreas and peripancreatic fluid accumulation, without biliary dilatation or microlithiasis. Both amylase and lipase in the blood were increased, with values of 132 U/L (reference, 0–180 U/L) and 382 U/L (reference, 0–180 U/L), respectively. Initial liver biochemical tests showed that transaminase, bilirubin, and albumin were normal. Serum calcium and triglyceride levels were 1.96 mmol/L (reference, 2.11–2.52 mmol/L) and 3.2 mmol/L (reference, <1.7 mmol/L), respectively. The Ransons score for pancreatitis was 5. He received treatment with somatostatin, proton pump inhibitors, and fluid replacement managed by balancing inflow with outflow. The volume of liquid in and out was balanced. Then, the patient complained of chest discomfort and shortness of breath. Chest CT on February 29 (day 4) showed multiple ground-glass opacities in both lungs. The test for COVID-19 infection by real-time polymerase chain reaction (PCR) assay was performed on March 1 (day 5) and returned positive. The peripheral blood lymphocyte count was slightly reduced to 0.86 $\times 10^9$/L (reference, 1.1–3.2 $\times 10^9$/L). CD4 and CD8 T cells in the blood were extremely low, with values of 196/μL (reference, 404–1612/μL) and 84/μL (reference, 220–1129/μL). Blood tests revealed that the patient's interleukin-6 was 29 861.4 pg/mL (reference, <10 pg/mL), D-dimer was 3.05 mg/L (reference, 0–0.55 mg/L), and C-reactive protein was >200 mg/L (reference, 1–10 mg/L). Water overload was excluded by bedside ultrasound examination and a normal result of brain natriuretic peptide. He was given arbidol capsule (200 mg 3 times daily) therapy. Oxygen inhalation was administered to the patient at 8 L/min via a nasal cannula. However, his dyspnea worsened. On the sixth day of the disease course, the patient suffered sudden cardiac arrest. After cardiopulmonary resuscitation and tracheal intubation, sedation therapy and mechanical ventilation were administered. The patient was then transferred to the intensive care unit. A chest radiograph on March 4 (day 8) displayed bilateral multiple infiltrating shadows and consolidation (Figure 1). He developed acute renal failure, and continuous renal replacement therapy was started on March 5 (day 9). Despite the use of a variety of vasoactive drugs and fluid resuscitation, the patient eventually died on day 10.

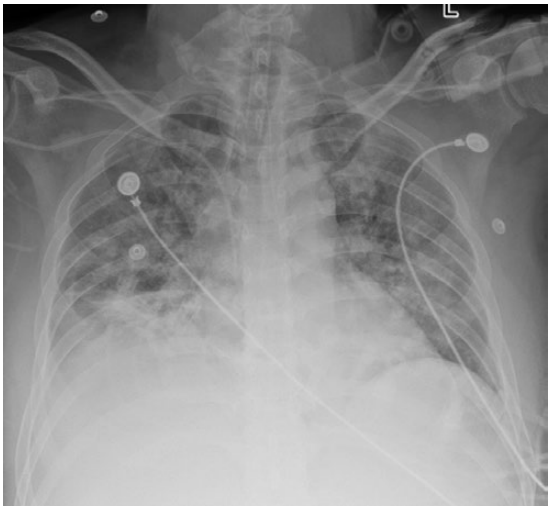

Figure 1. Chest x-ray of the first case on March 4, 2020 (day 8 of illness). The image shows bilateral multiple infiltrating shadow and consolidation.

Case 2

A 35-year-old male was admitted for 5 days of persistent upper abdominal pain with radiation to the back, nausea, and vomiting on March 23, 2020. He did not complain of fever, cough, dyspnea, fatigue, or diarrhea. He denied drinking, taking medicine, or overeating in recent days. He had no history of gallstones or autoimmune disease. Abdomen enhanced CT (Figure 2) on March 24 (day 6 of illness) showed pancreatic swelling, peripancreatic fluid accumulation, and prerenal fascial thickening without biliary dilatation or microlithiasis. Blood lipase was elevated, with a value of 1042 U/L (reference, 0–180 U/L), and amylase was normal. As he had had contact with residents of Wuhan recently, chest CT was performed, showing patchy shadows in the lower right lung and bilateral pleural effusion (Figure 2). COVID-19 infection was confirmed on March 24 (day 6) with PCR. His peripheral blood lymphocyte count was slightly diminished, with a value of 1.01 $\times 10^9$/L (reference, 1.1–3.2 $\times 10^9$/L). Blood tests revealed that his interleukin-6 was 498.13 pg/mL, D-dimer was 9.54 mg/L, and C-reactive protein was >200 mg/L. Initial liver biochemical tests showed that transaminase, bilirubin, and albumin were normal. Serum calcium and triglyceride levels were 1.92 mmol/L (reference, 2.11–2.52 mmol/L) and 3.97 mmol/L (reference, <1.7 mmol/L), respectively. CD4 and CD8 T cells in the blood were slightly reduced, with values of 385/μL (reference, 404–1612/μL) and 133/μL (reference, 220–1129/μL), respectively. In addition to enteral nutrition, he received somatostatin, proton pump inhibitors, and fluid replacement therapy. Arbidol was administered (200 mg 3 times daily) for antiviral treatment. The patient's symptoms improved gradually. Viral

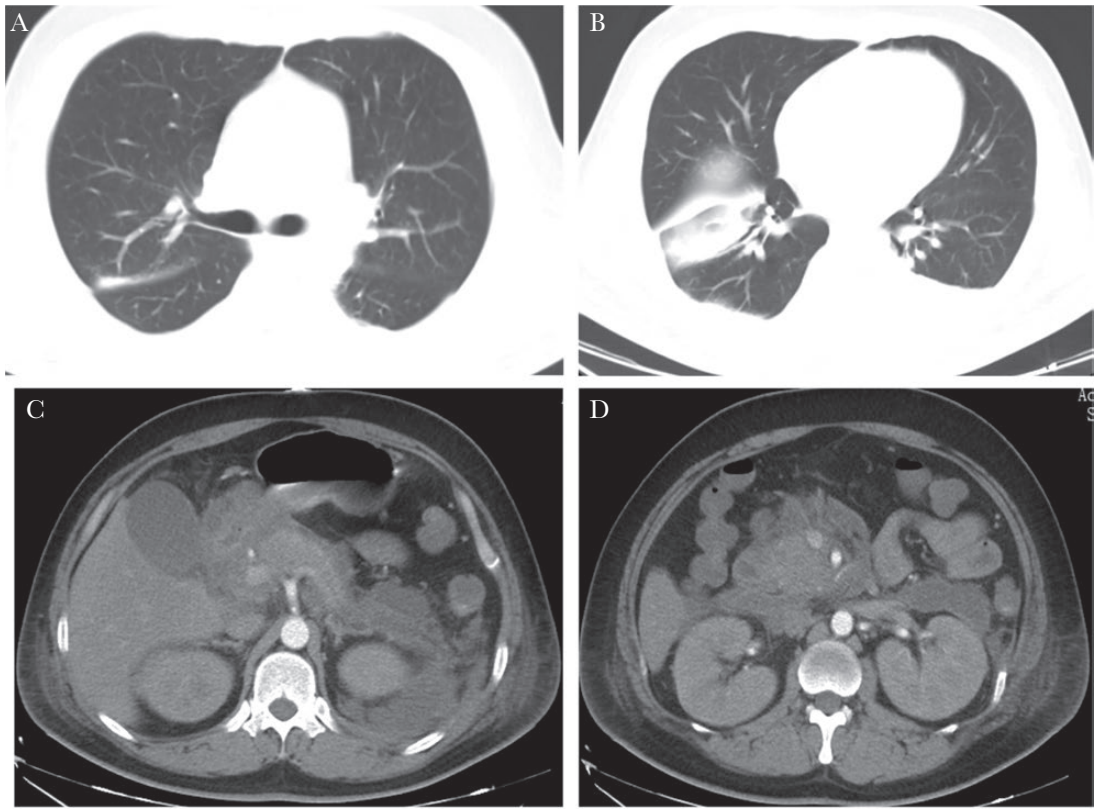

Figure 2. A and B, Chest axial computed tomography (CT) scan of the second case on March 24, 2020 (day 6 of illness). The images show patchy shadows in the lower right lung and bilateral pleural effusion. C and D, Abdomen enhanced axial CT scan of the second case on March 24, 2020 (day 6 of illness). The images show pancreas swelling and peripancreatic fluid accumulation, without common bile duct dilation and gallstone or microlithiasis.

RNA testing of nasal swabs and sputum by PCR turned negative on March 30 (day 12) and April 2 (day 15), respectively. He was discharged from the hospital in good condition on April 5.

DISCUSSION

In this study, we described 2 patients with COVID-19 who initially presented with persistent upper abdominal pain and nausea and were diagnosed with acute pancreatitis. Alternative etiologies for pancreatitis, including medication, gallstones, alcohol, and autoimmune or other more common etiologies were ruled out in these 2 patients. Patient 1 died of circulatory and acute renal failure. The second patient was discharged after showing significant improvement. Wang et al. reported that the incidence of pancreatic injury was 17% in patients with COVID-19 pneumonia, but they did not find any patients with acute pancreatitis [5]. Amer et al. reported 2 patients who were diagnosed with acute pancreatitis associated with SARS-CoV-2 [7]. Autopsy revealed that SARS-CoV-2 was detected in the tissues of the lung, liver, and heart, but whether the virus invades the pancreas is still unclear [9].

A spike protein encoded by the coronaviral genome is responsible for facilitating the entry of CoV into the target cell; analysis of the receptor-binding motif in the spike protein shows that most of the amino acid residues essential for receptor binding are conserved between SARS-CoV and SARS-CoV-2, suggesting that SARS-CoV-2 uses the same cell entry receptor, angiotensin-converting enzyme II (ACE2) [10, 11]. SARS-CoV has been detected not only in the tissues of the lung, liver, stomach, and kidney, but also in the pancreas, indicating that the pancreas is a potential coronaviral target [12]. ACE2 is highly expressed in the pancreas, and SARS-CoV enters the islets using ACE2 as its receptor and damages them, causing acute diabetes [13]. It has been reported that viral infection or immune factors are a rare cause of pancreatitis [14, 15]. This evidence suggests that coronavirus may directly cause pancreatic injury. Whether pancreatic injury is secondarily caused by hypoxia or immune damage secondary to the systemic inflammatory response is unclear.

Notably, the number of T cells in the peripheral blood was decreased in these 2 patients. A reduction of T cells is common in severe COVID-19, indicating that the novel coronavirus might mainly act on lymphocytes, especially T lymphocytes [16]. The T-cell count was extremely low in patient 1 after COVID-19 infection, and the patient died despite maximal mechanical ventilatory support and circulation support. A low T-cell count may be a surrogate for poor clinical outcomes.

CONCLUSIONS

Clinical data on COVID-19 with pancreatic injury are very limited. We reported 2 COVID-19 patients who initially presented with acute pancreatitis with different outcomes. Low T cells may indicate a poor outcome. The pathogenesis of acute pancreatitis caused by SARS-CoV-2 requires further research.

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Patient consent and ethical approval. Written informed consent was obtained from the patient or a legal representative. Ethical approval was granted by the ethics board of the Institute of People's Hospital of Wuhan University (WDRY2020-K068).

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