

CoViD-19 Infection and Acute Pancreatitis with Pancreatic Pseudocyst. Is There a Causal Relationship?

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Abstract

This report shows two cases of acute pancreatitis in CoViD-19 patients with development of pancreatic pseudocyst treated with lumen apposing stent and hypothesize on the possible cause-and-effect relationship between the infection and pancreatitis. Considering literature data and direct experience, it's possible that coronavirus causes a direct damage to pancreatic tissue.

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Abstract

This report shows two cases of acute pancreatitis in CoViD-19 patients with development of pancreatic pseudocyst treated with lumen apposing stent and hypothesize on the possible cause-and-effect relationship between the infection and pancreatitis. Considering literature data and direct experience, it's possible that coronavirus causes a direct damage to pancreatic tissue.

Key clinical message

This report shows two cases of acute pancreatitis in CoViD-19 patients with development of pancreatic pseudocyst treated with lumen apposing stent and hypothesize on the possible cause-and-effect relationship between the infection and pancreatitis.

Keywords : CoViD-19, SARS-CoV-2, Acute pancreatitis, pancreatic pseudocyst, lumen apposing stent

Introduction

Corona Virus Disease 2019 (CoViD-19) primarily involves respiratory system. However, digestive system involvement has been documented and different gastrointestinal manifestations were reported in up to 79% of the cases. Viral RNA has been isolated in the gastrointestinal tract of infected patients¹. Among them, cases of acute pancreatitis (AP) as the initial symptom were reported. We report two cases of AP developing pancreatic pseudocyst (PP) in CoViD-19 infected patients.

Case 1

A 62-years old male patient, complaining of severe abdominal pain radiating to the back and vomiting in the last 4 days, was admitted to the Emergency Unit. At entry, body temperature 36,6°C, blood pressure 135/85 mm Hg, heart rate 88 bpm, and oxygen saturation 94% at room air. Laboratory tests showed normal blood count and no signs of cholestasis, whilst an increase of C-reacting protein (12 mg/L; n. v. < 8 mg/L) and ESR 27 (mm/h; n. v. 1-19 mm/h), with a 4-fold increased levels of both amylase (534 U/L – n. v. 25-125 U/L) and lipase (326 U/L – n. v. 8-78 U/L). Abdominal ultra-sonography (US) showed pancreatic enlargement with multiple peri-pancreatic fluid collection in the body-tail area, normal bile ducts, and absence of biliary stones.

The real time polymerase chain reaction (RT-PCR) nasopharyngeal swab resulted positive for CoViD-19 and chest X-ray was negative without respiratory symptoms. The patient was admitted in CoViD Unit with diagnosis of AP in asymptomatic CoViD patient, and standard treatment for AP (fluid replacement, optimization of electrolyte balance) was started, requiring any treatment for his CoViD-19 infection. The medical history did not reveal potential aetiologies of AP.

Following 6 days, the patient developed acute symptoms with worsening abdominal pain, fever (39,8°C), chills, marked increase of ESR (85 mm/h) and C-reactive protein (215 mg/l), and leucocytosis (WBC 26.000 x 10³/UL; n. v. 4,8-10,8 x 10³/UL). The abdominal CT scan showed a large pancreatic pseudocyst (PP) (17x8x12 cm) developing in the anterior pancreatic body-tail area. Due to the development of recurrent, bulging vomiting, we decided, on the hospital day 9, to perform an endoscopic ultrasound-guided trans-gastric drainage of the pseudocyst and a Hot Axios 15 mm stent (Boston Scientific, Marlborough, MA, USA) was successfully placed (Figure 1A). Before the endoscopic procedure, the pseudocyst fluid sample was collected and the presence of Covid-19 confirmed by RT-PCR analysis with both AllplexTM 2019-nCoV (Seegene, Arrow Diagnostics, South Korea) and Quanty Covid-19 (Clonit, Italy) assays ².

Two weeks after stent placement, the pancreatic pathology recovered (Figure 1B). Following 2 negative molecular swabs, the patient was discharged from the hospital at day 26, with a planned US for stent removal.

Case 2

A 76 years-old male patient was admitted to Emergency Unit with mild dyspnea, cough, oxygen saturation of 91% on room air, and myalgias. CoViD-19 infection was discovered by a RT-PCR nasopharyngeal swab. Thoracic CT was negative for signs of CoViD pneumonia and patient was admitted in CoViD Unit requiring just oxygen therapy. No cortisone was administered.

Three days after, he developed severe epigastric pain radiating to the back, with nausea and vomiting. Laboratory tests showed elevated lipase (916 U/L; n. v. 25-125 U/L) and amylase (396 U/L; n. v. 8-78 U/L) levels. Abdominal US revealed pancreas diffusely enlarged, with low density, non-bordered peri-pancreatic collections in the body area, without focal lesions, normal gallbladder, common and intra-hepatic bile ducts,

and absence of biliary stones. AP diagnosis in CoViD patient was performed, and standard therapy with fluid and antibiotics was introduced. The medical history did not reveal potential aetiologies of AP.

Following 10 days, acute abdominal pain, nausea, vomiting, fever (39,2 °C), chills developed. Blood test revealed leucocytosis (WBC 31.000 x 10³/UL; n. v. 4,8-10,8 x 10³/UL), and increased of both ESR (87 mm/h) and C-reactive proteine (238 mg/L).

The abdominal CT scan showed a PP (11x6x9 cm) developing in the anterior pancreatic body area. An endoscopic ultrasound-guided trans-gastric drainage of the PP was performed and a Hot Spaxius 16 mm stent (Tae Woong Medical, Gojeong-ro, Wolgot-myeon, Gimpo-si, Gyeonggi-do, South Korea) was successfully placed (Figure 2 A, 2B).

The presence of Covid-19 in the aspirated fluid was confirmed by the same RT-PCR analyses performed in the other patient.

Ten days after, a TC scan control showed the regular stent placement and a reduction of more than 90% of the fluid collection diameter (Figure 2C). The patient had an uneventful recovery with gradual resolution of abdominal and pulmonary symptoms and was discharged 31 days following admission with a planned US for stent removal.

Discussion

The first report of pancreatic involvement in CoViD-19 infection described 9 patients in which receptor of angiotensin-converting enzyme 2 (ACE 2) was found to be expressed in both exocrine pancreas and islet^{3,4}. The proposed mechanism of pancreatic injury in CoViD-19 infection include a direct cytopathic effect mediated by local viral replication or a damage due to immune response with locoregional vasculitis and thrombotic microangiopathy, as occurs in other organs⁴.

In the lung the virus attaches to ACE 2 receptors and the spike protein (SP) attaches to alveolar cells, with a cytokine storm resulting in alveolar flooding and denudation of the lining epithelium, hampering oxygen exchange, and manifesting clinically as acute respiratory distress syndrome⁵. A similar mechanism may occur in the pancreas, where ACE 2 receptor expression and messenger RNA levels of ACE 2 are higher than in the lung³. Binding of the virus to ACE 2 receptor mediates pancreatic injury. To entry the pancreatic cells, SP needs ACE 2 as key receptor, and the priming of transmembrane protease serine 2 (TMPRSS2)⁶. Pancreatic injury is higher in severe CoViD-19 infection compared to milder disease, probably as consequence of the cytokine burst and immune dysregulated response⁷.

However, the causal role of CoViD-19 in pancreatitis development has been questioned^{8,9}.

We described two cases of mild CoViD-19 infection with development of AP with PP treated with endoscopic ultrasound-guided trans-gastric drainage by a lumen apposing stent. In both patients, other causes of AP, such as alcohol, drugs, trauma, ischemia, hypotension, previous thrombotic event, metabolic disorders, autoimmune diseases, toxins, iatrogenic events, or other viral infections, were excluded by an accurate anamnesis and evaluation of the personal health record. Furthermore, no therapies for CoViD-19, potentially responsible for AP, were performed. The detection of CoV-19 in the pseudocyst fluid, lead us to indicate the possible causal relationship between the viral infection and the development of AP. Moreover, the timing of the AP presentation, following the onset of CoViD-19, seems to be another important element.

In conclusion, the association between CoViD-19 infection and AP has been reported in several papers. However, it is crucial to differentiate between a simple coexistence and a causal relationship between these two pathologies. An unequivocal demonstration of this relationship should require a clear exclusion of any other known etiology, including drugs used in CoViD-19 treatment. Considering literature data and direct experience, we believe that a direct coronavirus damage to pancreatic tissue is possible, as demonstrated mainly by the finding of viral RNA in pancreatic pseudocyst fluid and, also, by the temporal association between the two pathologies, in case of lack of other etiologies. Anyway, our knowledge about this topic is

still limited and available data are difficult to interpret. Further experiences on wider series and multicenter cohort studies are needed to confirm our findings.

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Authors contribution

GG, AZ, RM conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript. AC, RM, MP conducted literature search on the topic, contributed to writing of discussion and revised the manuscript. MMF, GC, GL, GDDP supervised work and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Ethical Statement : Written informed consent was taken from the patients for the publication of cases report and images. This report does not contain any personal information that could lead to identification of the patients.

Data Availability Statement : The data that support the findings of this study are available on request from the authors. The data are not publicly available due to privacy and ethical restrictions.

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Figure legends:

Figure 1) a: EUS-guided trans-gastric drainage of the pseudocyst. b: CT scan control after 15 days from EUS-guided drainage.

Figure 2) a: Endoscopic view of the stent opening in the stomach. b: Radiologic control of the correct stent placement. c: CT scan control after 10 days from EUS-guided drainage.





