Case Report

Coronavirus Disease-19 as a New Etiology of Acute Pancreatitis: a Report of Two Cases and Literature Review

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ABSTRACT

Acute pancreatitis (AP) is a life-threatening condition for which a wide range of etiological factors are considered. While gallstones and alcohol consumption are the leading causative agents, infectious microorganisms are assumed to be involved in some AP cases. During the ongoing coronavirus disease-2019 (COVID-19) pandemic, a coincidence of mild AP and COVID-19 has been reported, and hereby, we present the first cases of COVID-19/AP comorbidity from Iran.

We present two cases of AP that occurred in patients with COVID-19 without any other risk factors with different outcomes. One of them had a mild AP and recovered, while the other patient suffered from a severe AP and expired. Also, it was noted that the first patient did not have any COVID-19 symptoms but abdominal pain, which probably was related to AP.

Conclusion: Based on this report, COVID-19 can be considered in the AP cases that do not have an underlying risk factor, regardless of the severity of AP and the presence of COVID-19 symptoms.

Keywords: COVID-19 pandemic, SARS-CoV-2, Acute pancreatitis

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INTRODUCTION

Considering the gastrointestinal differentials, excluding the diagnosis of acute pancreatitis (AP) as a life-threatening condition in a patient with an acute onset epigastric pain radiating to the back, along with nausea and vomiting, is critical (1). A wide range of etiological factors are considered to be associated with AP while, regarding their prevalence, gallstones and alcohol consumption are the leading causative agents (2). In approximately 10% of AP cases, infectious microorganisms, including viruses, bacteria, and parasites, are assumed to be involved (3). Among infectious causes of acute pancreatitis, viral agents, including hepatotropic virus, Cytomegalovirus, Coxsackie virus, Herpes simplex virus, Varicella-Zoster virus, Human Immunodeficiency virus, etc. compose the greatest number of infectious AP incidents (4). The ongoing coronavirus disease-2019 (COVID-19) pandemic, which is caused by severe acute respiratory

syndrome coronavirus 2 (SARS-CoV-2), has globally affected more than 21 million confirmed cases in a very short time (5). Although fever, cough, and shortness of breath are considered the main symptoms of the disease, increasing evidence of gastrointestinal manifestations such as nausea, vomiting, and diarrhea is confirmed (6,7). Additionally, pancreatitis has also been diagnosed in patients with COVID-19 without any other risk factors for pancreatitis. Exploring the distribution of SARS-CoV-2 receptor (angiotensin-converting enzyme 2 (ACE2)) in the pancreas, a study showed that SARS-CoV-2 can be associated with pancreatitis in some patients with COVID-19 (7-9). Herein, we report two cases of AP that occurred in patients with COVID-19 with different outcomes.

CASE REPORTS

Case 1: A 39-year-old man was referred to the clinic and then was admitted to Imam Khomeini Hospital, Kermanshah, Iran. He had progressive, moderate epigastric pain and nausea for 10 days. The pain was located in the epigastric zone, radiating to his back and other abdominal regions. It was neither positional nor did it change with eating meals. Except for his recent loss of appetite, he did not complain about recent symptoms of changed bowel habits, melena, weight loss, fever, or shivering. He adamantly denied any history of smoking, alcohol, or drug consumption. Additionally, any history of allergy, trauma, or other medical conditions was not present in this case. On physical examination, the patient was not toxic, his vital signs were normal, and he did not look pale or icteric. The abdomen was not distended, and no mass or organomegaly was palpable, although severe epigastric tenderness was detected. Other clinical examinations were normal. The abdominal ultrasonography was suggestive of pancreatitis, whereas no abnormalities of the gallbladder and biliary tract were detected. Laboratory tests revealed elevated (>3 times the upper limit of normal (ULN)) levels of lipase (180 IU/L) in favor of acute pancreatitis, elevated amylase (135 IU/L), elevated ESR levels, normal serological tests for autoimmune pancreatitis, and an unremarkable lipid profile (Table 1). Anti-acids and pancreatin were administered to the patient. After 2 days, his symptoms deteriorated, and computed tomography (CT) was performed, showing a diminished feathery pattern in the body and tail of the pancreas and a thin rhyme juxtaposing mesenteric fat, which were suggestive of pancreatitis. The patient was diagnosed with mild acute pancreatitis according to Atlanta criteria. Also, the usual causes of AP, like gallstones and alcohol consumption, were ruled out.

Taking a more detailed medical history, the patient revealed a history of close contact with a COVID-19-infected family member. In light of this evidence, the lung CT and reverse transcriptase-polymerase chain reaction (RT-PCR) tests were done, showing no lung involvement and a positive RT-PCR test for COVID-19 (Table 1). His condition started to improve after two days, and in the next follow-ups, all of his symptoms were diminished with normal pancreatic enzyme levels.

Case 2: The patient was a 63-year-old woman who presented to the emergency room of Imam Khomeini Hospital, Kermanshah, Iran, with a 2-day history of severe epigastric pain radiating to her back, headache, nausea, and vomiting that was not bloody. The pain got slightly relieved on leaning forward. In her medical history, she had a history of intrauterine device transplant (IUD), palpitation, and hypertension, for which she was on losartan and amlodipine. She gave no history of trauma, smoking, alcoholism, or drug abuse. On physical examination, the patient looked ill; her vital signs were normal, and her O_2 saturation was 92%. The abdominal examination revealed epigastric tenderness, whereas no abdominal distension or guarding was detected. In her admission laboratory workups, elevated (>3 times of ULN) levels of amylase (4060 IU/L) and lipase (1100 IU/L) confirmed the diagnosis of acute pancreatitis according to Atlanta criteria (Table 1). Ultrasonography on the first day of admission showed moderate fatty liver, normal gallbladder and biliary tract, and an increased diameter of the body of the pancreas. She received supportive treatments, including bowel rest, analgesia, and intravenous fluid resuscitation for acute pancreatitis. In the high-resolution CT (HRCT) on the third day of admission, global hypodensity and haziness of the body and the head of the pancreas, indicating an inflammatory process and pancreatitis, were detectable.

Although she had no recent history of fever, dyspnea,

Table 1. Laboratory tests at the time of admission.

Laboratory results	Case 1	Case2	normal range	units
Blood sugar	135	162		mg/dL
urea	22	25	15-45	mg%
creatinine	0.9	1.0	0.6-1.6	mg/dL
amylase	135	4060	100-28	IU/L
Lipase	190	1100	< 60	IU/L
Creatine kinase	76	86	24-195	IU/L
Sodium	140	141	135-145	mEq/L
potassium	4.3	4.3	5-3.5	mEq/L
Calcium	9	9.1	8.5-10.3	mEq/L
cholestrol	148	159	125-240	mg/dL
Triglyceride	141	124	40-200	mg/dL
High-density lipoprotein	42	40	35-70	mg/dL
Low-density lipoprotein	76	82	75-125	mg/dL
Albumine, serum	4.2	3.7	3.5-5.2	g/dL
Aspartate Aminotransferase	10	71	5-45	IU/L
Alanine Transaminase	18	22	5-45	ng/mL
Alkaline phosphatase	172	278	80-306	IU/L
Gamma-glutamyl Transferase	26	30	9-48	IU/L
Total bilirubin	0.5	0.9	0.1-1.2	mg/dL
Red blood cell count	5.09	5.32	4.5-5.8	× 106 /µg
White blood cell count	10.68	12.4	4.0-10.0	× 1000/cum
Hemoglubin	13.5	13.9	12-17	g/dL
Hematocrit	40.3	45.2	42-50	%
Mean corpuscular volume	79.2	86.59	80-100	Fl
Mean corpuscular hemoglubin	26.4	26.63	27-33	Pg
Mean corpuscular hemoglobin concentration	33.4	30.75	31-36	g/dL
Platelet	340	276	150-450	× 10^3 / µg
Lymphocytes	25	42	11.0-49.0	%
Polymorphonuclear neutrophils	65	48		%
Monocytes	7	8		%
Eosinophils	3	2		%
Erythrocyte sedimentation rate	34	67	0-30	mm/hour
C-reactive protein	+	++		
Serum Immunoglobulin G	1221	1053	670-1850	mg/dL
Human Immunodeficiency virus Antibody (I + II)	Non-reactive	Non-reactive		

or myalgia, she gave a suspicious history of recent dry coughing, and her lung HRCT scan revealed multifocal bilateral ground-glass opacities in favor of COVID-19. Later, RT-PCR for COVID-19 was found to be positive. Just like the first patient, gallstones and alcohol consumption were ruled out.

In the following days, the patient's condition deteriorated. She got a fever, generalized edema, ascites, high blood glucose levels (in favor of pancreatitis-induced diabetes), and moderate epigastric pain. The repeated ultrasound

study revealed increased diameter and heterogenic echo of the pancreas, a 47-millimeter (mm) hypoechoic region superior to the pancreatic body, a similar focus with a 42 mm diameter in the inferior side of the pancreatic tail, and free fluid accumulation around the spleen also in perihepatic space was diagnosed. The following contrast abdominal CT revealed a non-enhancing accumulation in the lesser sac, providing evidence for primary stages of pseudo-cyst formation. Broad-spectrum antibiotics were administered, and she was transferred to the intensive care unit (ICU). On the following control CT, necrotizing pancreatitis and increased size of the accumulation in the lesser sac, along with free fluid accumulation in the abdomen, were remarked. Considering her worsening condition and the growing size of the accumulation, interventions for cyst drainage were done. Following the procedure, after a short-term relief, the patient presented with fever (38.4° C), hypotension (85/pulse), tachycardia (heart rate: 120), fluid overload, and edema. Her laboratory tests, summarized in Table 1, showed anemia, thrombocytopenia, metabolic acidosis, slightly raised creatinine level, elevated amylase, liver enzymes, and INR level, providing evidence for the diagnosis of a septic shock and disseminated intravascular coagulation (DIC). The patient did not respond to resuscitation and expired on the first day of her second admission.

DISCUSSION

According to Atlanta criteria, AP is clinically defined as the existence of two out of three of the following criteria in the patient: acute onset persistent abdominal pain located in the epigastric region mostly radiating to the back, more than three times ULN increase in serum lipase (or amylase) activity, along with characteristic findings of AP on CT or magnetic resonance imaging (MRI). Both of the presented cases matched the criteria and were diagnosed with AP. In *case 1* the severity of AP is estimated as mild due to the absence of local or systemic complications. Also, the latter case is described as severe because of presented local and systemic complications (2). Finding out the etiology of AP partially drives early management and follow-up strategy (10). Concomitant COVID-19, in the absence of other etiological factors, can potentially provide evidence for COVID-19-induced AP, having the important role of viral agents in infectious causes of acute pancreatitis in mind (4). Considering the fact that the presented patients did not have the usual predisposing factors of AP and they were positive in RT-PCR and lung HRCT-scan, it may be assumed that the most probable cause of the AP was COVID-19. Recent case reports have suggested COVID-19 as AP etiology(6). Providing evidence for COVID-19-induced AP, the study of Wang and others showed a 17% incidence of pancreatic injury among the 52 patients with COVID-19 pneumonia (8). Although the potential of this virus to cause AP is yet to be illustrated.

Detecting the SARS-CoV (2003) virus in the pancreas along with the expression of ACE2 SARS-CoV receptors in the islets, suggests that the pancreas is potentially a coronaviral target (11,12). Hypothetically, COVID-19-induced acute pancreatitis is either mediated by a direct cytopathic injury by local SARS-CoV-2 replication or indirectly through a harmful immune response induced by the infection (8).

To the best of our knowledge, in previous studies regarding the presence of obvious symptoms in favor of COVID-19, the importance of AP evaluation in patients with COVID-19 experiencing unexplained abdominal pain has been suggested (13,14). Also, it is worth mentioning here that viral pancreatitis has been mostly represented with mild symptoms (8), whereas the patient of *case 2* presented symptoms of severe pancreatitis. Finally, considering the absence of any symptoms in *case 1* in favor of COVID-19 and the presence of AP accompanying a positive test for COVID-19, this study suggests the investigation of COVID-19 in patients with AP when all other etiologies are rolled out during the ongoing pandemic. Unlike other publications, we showed that COVID-19 can be considered the causative agent of severe AP.

CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

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