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Case of COVID-19 Presenting with Acute Pancreatitis and Acute Appendicitis

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Abstract

Coronavirus disease 2019 (COVID-19) may present as an acute abdomen of obscure pathophysiology. We report a case of a 32-year-old man presented with an acute abdomen who had diagnosed COVID-19 infection at emergency department one week ago. Physical examination revealed abdominal tenderness accompanying guarding and rebound. Other systemic examination, including the respiratory system, were unremarkable. Blood sample was obtained and the patient was evaluated via abdominal computed tomography (CT) scan that exhibited acute appendicitis and pancreatitis. The patient was referred to tertiary hospital for surgery. Coexistence of acute pancreatitis and appendicitis is a rare condition, furthermore we could not attain any literature in relation to this coexistence in COVID-19.

1. Introduction

Scarce data exist about the presentation of COVID-19 as an acute abdomen; in most case reports, no definitive underlying pathology is documented. Emerging epidemiological data on COVID-19 indicate that there is a relationship between gastrointestinal injury and SARS-CoV-2 infection [1]. The pathogenic mechanism which causes multi-organ dysfunction, is not understood completely. In almost all COVID-19 cases, viral nucleocapsid protein has been verified in the gastrointestinal lumen apart from the esophagus and rectum [1]. Angiotensin-converting enzyme II (ACE II) receptor expression is not only presented in the lungs besides, it is widely expressed at various kinds of cells as the esophageal epithelial cells, enterocytes of the ileum and colon, cardiovascular, renal, pancreas and adipose tissue [2]. The virus attaches to extra-pulmonary tissues by ACEII receptors; therefore, gastrointestinal manifestations can be explained by this pathway in COVID-19.

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2. Case Presentation

Our case was a 32-year-old man who applied to the emergency department two times in that week. At first presentation he had a cough and fever. Thorax CT scan, routine biochemistry laboratory tests and nasopharyngeal swab for COVID-19 were performed to evaluate pneumonia and etiology. CT scan revealed that no pneumonia indication. Mild elevated CRP in serum and increased white blood cells in the blood sample was detected. COVID-19 infection via real-time PCR was found positive. Favipiravir, which is an antiviral drug that selectively inhibits the RNA-dependent RNA polymerase of influenza virus [3] and thought to has potential contribution to the healing process of COVID-19 infection, was prescribed.

Five days later, at the second admission, he complained about a 2- or 3-days history of vague, right lower quadrant and epigastric abdominal pain that was severe on the day of admission. Physical examination revealed abdominal tenderness with guarding and rebound. Other systemic examination, including the respiratory system, were unremarkable. The saturation of peripheral oxygen (SpO2) was 98% on room air; heart rate was 92 beats per minute, and blood pressure was 110/75 mm Hg. Infection markers such as C-reactive protein (CRP), white blood cells were high at initial laboratory tests and also mild to moderate elevation of serum amylase observed. (TABLE 1) An abdominal CT scan was performed for further evaluation. CT scan demonstrated that the appendix diameter was 11 mm, wall thickening and contrast enhancement. Moreover, the peripancreatic area was edematous without necrosis. According to radiological findings, acute appendicitis and pancreatitis were diagnosed. (FIG. 1)

TABLE 1. **Biochemistry and CBC Results.**

Parameters		**Normal Range Units**	**First Presentation**	**Second Presentation**	**Pre Operation**
Biochemistry	**Glucose**	(70-99) mg/dl	98	90	96
	Creatinine	(0.7-1.3) mg/dl	1.2	1.05	1.03
	Urea	(19-49) mg/dl	24	34	30
	Total Protein	(66-83) g/l	78	78	68
	Albumin	(35-52) g/l	46	44	47
	ALT	(<50) U/l	40	29	30
	AST	(<50) U/l	39	46	32
	GGT	(<64) U/l	62	58	47
	Total Bilirubin	(0.3-1.2) mg/dl	0.35	0.84	0.7
	Direct Bilirubin	(0-0.2) mg/dl	0.15	0.09	0.1
	Amylase	(28-100) U/l	104	236	152
	Lipase	(<50) U/l			108
	CRP	(0-5) mg/dl	59	153	170
	Ferritin	(22-322) µg/l	297	320	334
CBC	**White Blood Cell**	(*10^9)/l	14	16.8	15.66
	% Neutrophil	(42-77) %	74.2	81.8	83.9

	% Lymphocyte	(20-44) %	14.6	8.9	9.4
	% Monocyte	(2-9.5) %	9.4	8.0	5.0
	% Basophil	(0-1.75) %	0.3	0.5	0.2
	% Eosinophil	(0.5-5.5) %	0.2	0.8	0.7
	Hemoglobin	(13.5-17.5) mg/dl	15.8	14.7	13.5
	Hematocrit	(39.5-50.5) %	45.8	44.9	38.7
	Platelet	(*10^9)/l	273	210	166

CBC: Complete blood count

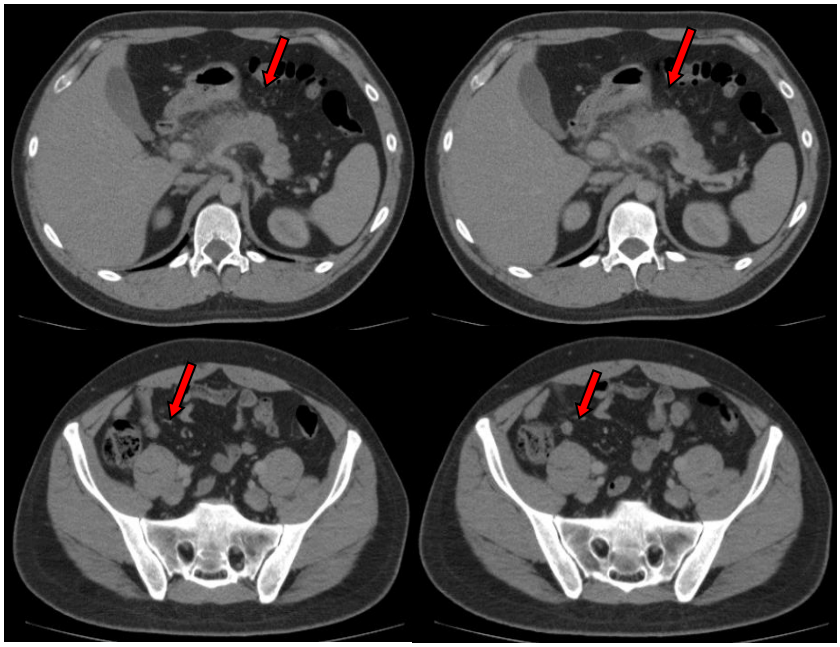

FIG. 1. **CT Scan Images (Pancreatitis, Appendicitis).**

The patient was referred to a tertiary hospital for surgery and underwent appendectomy without any complications. He was discharged from the hospital two days after the surgery.

3. Discussion

Multiple case reports have reported acute pancreatitis or appendicitis in the setting of COVID-19 infection. We are not aware of previous case reports that coexisting acute appendicitis and pancreatitis in COVID-19 positive patients. In the literature research, an only scientific letter could be found that stating a 6 years old pediatric patient who had pancreatitis and appendicitis caused by influenza infection [4].

Various microorganisms such as viruses, bacteria and fungi may cause acute pancreatitis. Hepatotropic viruses such as Hepatitis A, B and E, coxsackie viruses, human immunodeficiency virus, herpes simplex virus, varicella-zoster virus had been detected in acute pancreatitis cases so far [5].

According to the Revised Atlanta Classification, to diagnosis of acute pancreatitis requires at least two of the following features: Typical abdominal pain; elevated amylase or lipase (>3 times the upper limit of normal) and radiographic evidence [6]. Elevated amylase or lipase should be interpreted cautiously. These parameters are not exclusive indicators of pancreatic injury. Mild increases of these parameters can be explained by misbalance of productions and clearance of these parameters. Both amylase and lipase are cleared by the kidneys [7]. Acute or chronic kidney diseases can be the reason of raise amylase and lipase because of the decrease clearance. Amylase is not only secreted by the pancreas, it is also secreted by salivary gland, normal and diseased lung tissue [7]. Based on this; if the lung tissue or salivary glands are affected, elevated amylase in blood serum, can be detected. Lung tissues are generally affected by ACEII receptors in COVID-19 infections. Gastroenteritis is a well-known cause of pancreatic enzyme elevation in the blood serum [8]. Gnadinger MP et al, has suggested a hypothesis that Intestinal permeability could be increase for macromolecules such as amylase in acute gastroenteritis because of the intestinal inflammation [9]. Thus, increased lipase and amylase are not specific indicators of pancreatic injury.

According to the Revised Atlanta Classification, acute pancreatitis was diagnosed for this patient. The patient had abdominal pain which started in the umbilical area and referred to the right hypochondriac and epigastric region. Therefore, the first criterion was met by the description of pain. Since the pancreatic enzymes were just elevated above two-fold upper limits of normal, the second criterion was not met. The patient applied to the emergency department two times in a week. He was complaining about cough and fever in the first presentation. Biochemical parameters including amylase and lipase were in the normal range and no pneumonia criteria was detected. Therefore, he was discharged by favipiravir prescription. In the second presentation, the patient was suffering from abdominal pain which endured a few days and augmented over time. Biochemical tests revealed that two-fold elevated pancreatic enzymes and increased infection markers. Renal function tests were entirely normal and there was no evidence that clearance of pancreatic enzymes was reduced. When test results and anamnesis are considered, the source of the pancreatic enzyme in the serum should be due to a pancreatic injury. Finally, the CT scan revealed inflammation of the pancreatic area without necrosis and the third criterion was met.

ACE II receptor expression is not only present in the lungs. This receptor is widely expressed at various kinds of cells such as the esophageal epithelial cells, enterocytes of the ileum and colon also cardiovascular, renal, pancreatic and adipose tissue [2]. In COVID-19 patients, viral nucleocapsid protein has been verified in almost the entirety of the gastrointestinal lumen apart from the esophagus to the rectum [1]. Digestive symptoms may be occurred in COVID-19 infections by direct virus invasions of the target cell or immune-mediated end-organ injury [10]. Attachment of virus to extra-pulmonary tissues by ACEII receptor causes to induce lipotoxicity and cytokine storm. Thus, this pathway could be one of the explanation of pancreatic injury [11]. Clinical research demonstrates that cytokine profiles such as IL-6, IL-8, and IL-10 of acute pancreatitis and COVID-19 infections have been found similar [12].

Appendicitis, inflammation of the vermiform appendix, is the most common abdominal surgical emergency in the world. Appendicitis can lead to abscess, ileus, peritonitis, or death if it is not treated properly [13]. Although, various theories exist about the cause of appendicitis, there is no decisive consensus. The predominant theory?? is luminal obstruction of the appendix. The obstruction causes failure to drainage of secretions and increases luminal pressure that leads to ischemia of the appendix wall. Hyperplasia of the lymphoid tissue in the mucosa or submucosa, caused by bacterial, viral, fungal, parasitic

infections or other inflammatory bowel diseases, has been considered as the most common mechanism causing obstruction of the appendix lumen [13].

ACE inhibitors and angiotensin receptor blockers (ARB) are generally well-tolerated drugs. ACE inhibitors can lead edema of the small intestine by a probable similar mechanism with orofacial manifestations [14]. ACE inhibition provokes to the accumulation of bradykinin and substance P in the plasma or tissues by reducing these autacoids' metabolism. Kenneth J.M et al have pronounced a hypothesis that small-bowel angioedema can be the reason for appendicitis and if ACE inhibition causes small-bowel angioedema, appendicitis should be much more common in patients using ACE inhibitors or ARB [15]. According to their retrospective cohort study, they concluded that; using renin-angiotensin system blockers was associated with a greater risk for appendicitis [15]. However, it requires further studies, the same pathway could be contemplated for our case as well.

Studies designate that ACE receptor pathway contributes to the pathophysiological process in acute appendicitis and pancreatitis. Therefore, our hypothesis is that coexistence of acute appendicitis and pancreatitis in our case, may not be just a coincidence.

4. Conclusion

We documented that the coexistence of pancreatitis and appendicitis may be presented in COVID-19 infection. Further research about how COVID-19 infection affects the gastrointestinal system might help to illustrate the pathophysiology of appendicitis and pancreatitis better.

5. Funding

None.

6. Conflict of Interest

The authors have no commercial associations or sources of support that might pose a conflict of interest.

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