COVID-19 associated Acute Necrotizing Pancreatitis with Normal Serum Amylase and Lipase levels: Report of An Unusual Finding.

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Abstract

Coronaviruses are a large family of single-stranded RNA viruses infecting humans and animals, causing a multitude of symptoms. Since its outbreak, coronavirus not only affects the respiratory system but shows unusual gastrointestinal complications as well. Pancreatitis is known to be caused by biliary stones, alcohol abuse, viruses, drug intake, metabolic syndromes or trauma. Diagnosis of acute pancreatitis requires any two of the three criteria: acute onset of severe upper abdominal pain, consistent with pancreatitis; elevation of serum amylase or lipase, three times the upper limit of normal; characteristic imaging findings. COVID-19 pancreatitis is thought to be mediated by angiotensin-converting enzyme-2 receptor on the host cells, which are highly expressed in the pancreatic cells. Here, we report a unique case of acute necrotizing pancreatitis caused by COVID-19 with hyperglycemia, normal amylase and lipase levels.

Introduction

Corona viruses are a family of single-stranded RNA viruses causing infections in animals and humans (1). COVID-19 is caused by novel coronavirus SARS-CoV2. Since the onset of pandemic, a wide spectrum of gastrointenstinal complications and few cases of acute pancreatitis have been reported in the literature in association with COVID-19 infection (1). Here, we report a unique case of acute necrotizing pancreatitis caused by COVID-19 with hyperglycemia, normal amylase and lipase levels.

Case Report

A 35 years old male presented to the Emergency Department with complaints of abdominal pain, fever and mild cough for 5 days. He was not an alcoholic and had no history of trauma. No history of any chronic disease or medication. On examination, he was febrile with tenderness in the epigastric region and oxygen saturation was maintained. Laboratory investigations revealed normal serum amylase - 46 U/L (Units per Litre); lipase - 42 U/L. Gamma-Glutamyl Transferase (GGT) was elevated (149 U/L). Otherwise liver function tests were normal. Random blood glucose was elevated (240 mg/dl). Serum calcium (9 mg/dl) and lipid profile (triglycerides - 130 mg/dl) were normal. Patient was subjected to Contrast Enhanced Computed Tomography (CECT) abdomen, which showed non-enhancing necrotic areas involving the tail of pancreas with fluid and fat stranding in the peripancreatic spaces and thickening of the adjacent fascial planes. Rest of the pancreas was unremarkable. Bilateral minimal pleural effusion was noted. Diagnosis of acute necrotizing pancreatitis was given on imaging (Modified CT severity index – 8/10) [Figure 1A & B]. No cholelithiasis or choledocholithiasis was seen on CT. Visualized base of lungs showed ground glass opacities and interstitial septal thickening. The patient was then subjected to dedicated CT chest which

revealed bilateral confluent and discrete, subpleural and peribronchovascular consolidations with ground glass opacities [Figure 2A-C]. In view of the typical imaging findings for COVID-19, patient underwent Reverse transcription polymerase chain reaction (RT-PCR) for COVID-19, which turned out to be positive. Initially, he was treated conservatively with bowel rest, analgesics, intravenous fluid resuscitation, and empirical antibiotics. Serum amylase and lipase levels were repeated the next day, which were also within normal limits. The patient's symptoms gradually improved and was discharged.

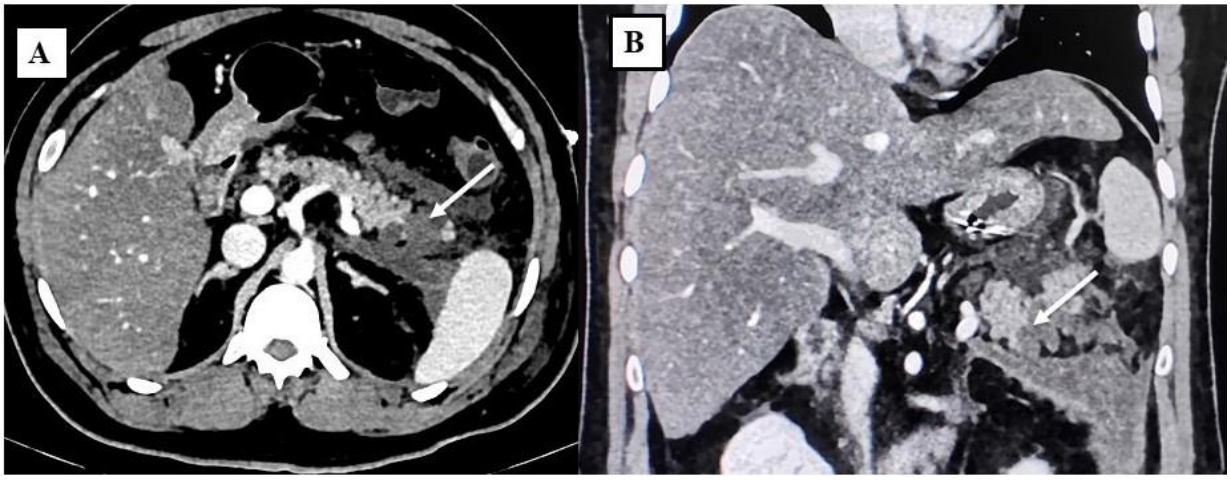

Figure 1: CECT abdomen axial section shows non-enhancing hypo-attenuating necrotic collection involving the tail of pancreas (white arrow) with extension into left anterior peripancreatic and pararenal spaces.

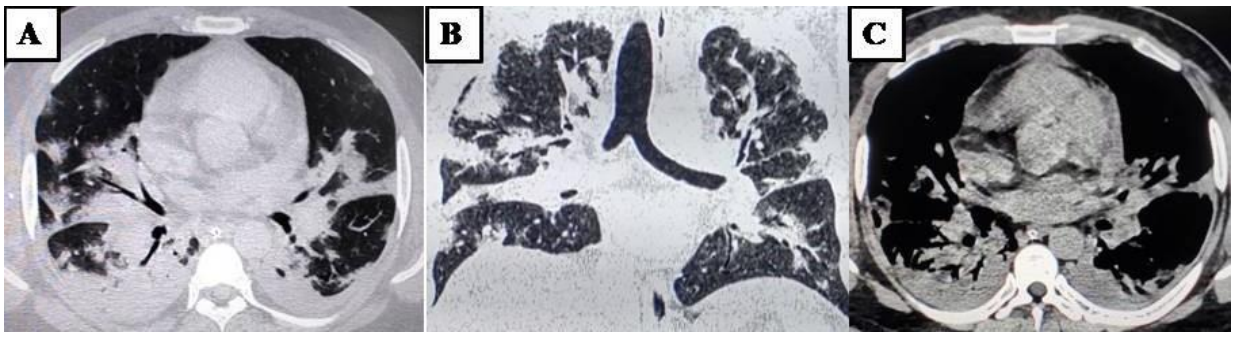

Figure 2: HRCT chest lung window, axial & coronal sections (A & B) show multiple confluent and discrete, mixed subpleural and peribronchovascular consolidations with ground

glass opacities and interstitial septal thickening involving both lungs. HRCT chest mediastinal window, axial section (C) shows bilateral pleural effusion.

Discussion

Acute pancreatitis is caused by various etiologies that includegallstones, alcohol abuse, hypertriglyceridemia, hypercalcemia, iatrogenic causes, infections, autoimmune and hereditary conditions, chronic medications and trauma (2). A wide range of bacterial, viral, fungal and parasitic organisms can cause pancreatitis. Mumps, coxsackie, measles and Hepatitis viruses have been historically implicated in causing pancreatitis (3). Diagnosis of acute pancreatitis requires any two of the three criteria: acute onset of severe upper abdominal pain, consistent with pancreatitis; elevation of serum amylase or lipase, three times the upper limit of normal and characteristic imaging findings (4). CECT abdomen has very high sensitivity and specificity of 90% for diagnosis of pancreatitis (5). Revised Atlanta classification categorizes acute pancreatitis into interstitial edematous and necrotizing pancreatitis based on imaging findings. Acute necrotizing pancreatitis typically occurs by 48-72 hrs after the disease onset (6). Our patient had typical abdominal pain and imaging showed pancreatic necrosis with peripancreatic inflammation and collection leading us to the diagnosis of acute necrotizing pancreatitis. A study states that CT is less sensitive in picking the necrosis before 4 days of onset (7). CECT is generally recommended after 4- 5 days of onset when the necrosis starts to appear radiologically (8). Our case had mild non-enhancing necrotic areas only in the tail region. So we presume that CT was showing early phase of necrosis. CT chest revealed ground-glass opacities and consolidation, which were proven to be secondary to COVID-19 by RT-PCR. Our patient had no history of alcohol intake, trauma, medications or any prior interventions with normal triglyceride and calcium values and CT

abdomen showing no evidence of biliary stones. Since CT chest findings and RT-PCR confirmed COVID-19, we ascertain that acute necrotizing pancreatitis was also caused by COVID-19 infection.

COVID-19 pancreatitis is thought to be mediated by angiotensin-converting enzyme-2 (ACE-2) receptor on the host cells, which are highly expressed in the pancreatic cells (9). Possible pathogenesis include direct cytopathic effect of local viral replication or by the immune response induced by the virus indirectly. Our case had a unique finding that serum amylase and lipase levels were not elevated, both at admission and the next day. Serum amylase has low specificity and can be elevated in various conditions like cholecystitis and also be normal in alcohol and hypertriglyceridemia induced pancreatitis (10). Lipase is produced and stored in pancreatic acinar cells, hence it is very specific and has a negative predictive of 94 – 100% in diagnosing pancreatitis (11). Literature shows that lipase increase within 4-8 hours of onset of acute pancreatitis to peak at 24 hours. Amylase rise after 6-24 hours to peak at 48 hours. These enzymes stay elevated in the blood stream for about 7-14 days. However, in our case, it was peculiar to note the normal enzyme levels inspite of the ongoing infective and inflammatory processes (12). Many isolated case reports have documented that acute pancreatitis can have normal lipase levels (4,5,10,11). In cases of acute on chronic pancreatitis, both amylase and lipase levels may remain normal due to loss of secretory function after chronic inflammation and fibrosis of the gland. In the case series of COVID-19 associated pancreatitis published by Wang et al, three of the patients had elevated amylase but normal lipase levels (13). To the best of our knowledge, this is the first case of COVID-19 pancreatitis which had both normal lipase and amylase levels.

Another finding in our case was hyperglycemia. Hyperglycemia in a COVID patient with pancreatitis could be due to direct cytopathic effect of the virus, as the islet cells are more concentrated in the pancreatic tail region and also show high expression of the ACE-2

receptors (14). Other possible reasons for hyperglycemia include stress induced transient hyperglycemia and incidentally detected pre-existing diabetes (15). Diabetes workup including HbA1c assay may be useful in ascertaining the cause of hyperglycemia. Identifying the COVID-19 patients with pancreatitis is of paramount importance as they usually have a severe illness on admissionand multisystem involvement with acclerated clinical course. Including the upper abdomen in CT chest plain study for COVID pneumonia also helps in early identification of pancreatitis. CECT plays an important role in confirming the diagnosis and identification of necrosis, assesment of severity and in initiating the appropriate treatment.

Conclusion

COVID-19 patients can present as acute pancreatitis with normal serum amylase and lipase levels. Emergency physicians should be aware of this diagnostic conundrum and should have a high index of suspicion in patients presenting with acute abdominal pain during this pandemic and set a low threshold for further evaluation with imaging.

References:

1. Teresa Gipson, MD, and suzanne P. Lee, MD, University of Rochester School of Medicine, Rochester, New York. Am Fam Physician. 2007 May 15; 75(10):1513-1520.
2. Chatila AT, Bilal M, Guturu P. Evaluation and management of acute pancreatitis. World J Clin Cases. 2019; 7(9):1006-1020.

3. Rawla P, Bandaru SS, Vellipuram AR. Review of Infectious Etiology of Acute Pancreatitis. Gastroenterology Res. 2017; 10(3):153-158.
4. Singh A, Shrestha M, Anand C. Acute pancreatitis with normal amylase and lipase--an ED dilemma. Am J Emerg Med. 2016 May;34(5):940.e5-7. doi: 10.1016/j.ajem.2015.10.026. Epub 2015 Oct 23. PMID: 26521195.
5. Cartier T, Sogni P, Perruche F, et al. Normal lipase serum level in acute pancreatitis: a case report. Emerg Med J. 2006;23(9):701-702. doi:10.1136/emj.2006.037655.
6. Shyu J, Sainani N, Sahni V et al. Necrotizing Pancreatitis: Diagnosis, Imaging, and Intervention. RadioGraphics. 2014;34(5):1218-1239. doi:10.1148/rg.345130012
7. Spanier BW, Nio Y, van der Hulst RW, Tuynman HA, Dijkgraaf MG, Bruno MJ. Practice and yield of early CT scan in acute pancreatitis: a Dutch Observational Multicenter Study. Pancreatology. 2010;10(2-3):222-8. doi: 10.1159/000243731.
8. Rashid MU, Hussain I, Jehanzeb S, et al. Pancreatic necrosis: Complications and changing trend of treatment. World J Gastrointest Surg. 2019;11(4):198-217. doi:10.4240/wjgs.v11.i4.198.
9. Kataria S, Sharif A, Ur Rehman A, et al. (July 13, 2020) COVID-19 Induced Acute Pancreatitis: A Case Report and Literature Review. Cureus 12(7): e9169. doi:10.7759/cureus.9169
10. Arvind K Mathur, Angela Whitaker, Hemchand Kolli1, Trinh Nguyen2 Acute Pancreatitis with Normal Serum Lipase and Amylase: A Rare Presentation JOP. J Pancreas (Online) 2016 Jan 08; 17(1):98-101.
11. Shah AM, Eddi R, Kothari ST, Maksoud C, DiGiacomo WS, Baddoura W. Acute pancreatitis with normal serum lipase: a case series. JOP. 2010 Jul 5;11(4):369-72. PMID: 20601812.

12. Jasdanwala S, Babyatsky M (2015) A critical evaluation of serum lipase and amylase as diagnostic tests for acute pancreatitis. Integr Mol Med 2: DOI: 10.15761/IMM.1000137
13. Wang F, Wang H, Fan J, Zhang Y, Wang H, Zhao Q: Pancreatic injury patterns in patients with coronavirus disease 19 pneumonia Gastroenterology. 2020, 10.1053/j.gastro.2020.03.055.
14. Wang X, Misawa R, Zielinski MC, Cowen P, Jo J, Periwal V, Ricordi C et al Regional differences in islet distribution in the human pancreas--preferential beta-cell loss in the head region in patients with type 2 diabetes. PLoS One. 2013 Jun 24;8(6):e67454. doi: 10.1371/journal.pone.0067454. PMID: 23826303; PMCID: PMC3691162.
15. Thaweerat W. Current evidence on pancreatic involvement in SARS-CoV-2 infection. Pancreatology. 2020;20(5):1013-1014. doi:10.1016/j.pan.2020.05.015