



# Pancreatitis in Pediatric Patients With COVID-19

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## INTRODUCTION

Over the past several months, understanding of the novel coronavirus disease 2019 (COVID-19) has grown extensively with new findings of organ system involvement reported on a regular basis. Pulmonary manifestations of the disease appear to be the most common presentation of COVID-19, but extrapulmonary disease including gastrointestinal symptomatology are becoming more apparent. To date, the association between COVID-19 and pancreatitis has been limited to a few case reports, mostly in adult patients. This case series illustrates the clinical presentation of 3 pediatric patients who were diagnosed with pancreatitis about a week after the onset of COVID-19 symptoms. Diagnosis of pancreatitis was based on 2 of 3 following criteria: (1) abdominal pain, (2) amylase and lipase elevated over 3 times the upper limit of normal, and/or (3) abdominal imaging consistent with pancreatitis [1]. Although the direct causation is hard to prove, the temporal association does suggest the relationship between severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and pancreatitis in children.

## CASE 1

A previously healthy, obese, 15-year-old male presented to the emergency department with non-bloody, non-bilious vomiting, worsening epigastric abdominal pain, and fever that began on the day of presentation. He reported a week of nasal congestion, anosmia, and ageusia. On examination, he was hemodynamically stable with mild tenderness to palpation of the epigastric region and no signs of respiratory distress. Initial laboratory studies demonstrated a normal white blood cell count of  $4.5 \times 10^3/\mu\text{L}$  with 18.6% lymphocytes, c-reactive protein (CRP) of

1.47 mg/dL, and sedimentation rate (ESR) of 4 mm/h. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were slightly elevated to 53 and 86 U/L, respectively, and his lipase was elevated to 233 U/L. His glycated hemoglobin test (hemoglobin A1C) and triglycerides were within the normal range. An abdominal computed tomography (CT) demonstrated mild stranding around the head of the pancreas and proximal duodenum with scattered ground-glass opacities in bilateral lower lung fields (See Table 1). Based on the laboratory results and abdominal imaging, he was diagnosed with acute pancreatitis. Due to symptoms of anosmia and ageusia and lower lung field findings on imaging, a SARS-CoV-2 real-time reverse transcription-polymerase chain reaction (RT-PCR) was performed, which was positive confirming the diagnosis of COVID-19. He was admitted and placed on intravenous fluids and a liquid diet and prescribed pain medications to ease his abdominal pain. He was discharged on day 3 of admission with resolution of abdominal pain, improving lipase level, and tolerating a normal diet. There were no signs of respiratory distress throughout his entire hospitalization.

## CASE 2

A previously healthy, overweight, 11-year-old male presented to the emergency department with periumbilical abdominal pain and poor oral intake for 2 days. He also reported headache, chills, tactile fever, and intermittent hematochezia and epistaxis of 8 days duration prior to presentation. He was tested for SARS-CoV-2 antibodies by his pediatrician 6 days into his illness (2 days prior to admission) and was found to be positive. On physical exam, he was noted to be hemodynamically stable with epigastric tenderness but no signs of respiratory distress. Initial laboratory studies demonstrated mild leukocytosis of  $8.4 \times 10^3/\mu\text{L}$  with 17.3% lymphocytes, mild thrombocytopenia to  $140 \times 10^3/\mu\text{L}$ , CRP of 24.11 mg/dL, and ESR of 99 mm/h. AST and ALT were slightly elevated (47 and 54 U/L, respectively), and amylase and lipase were elevated to 156 and 582 U/L, respectively. His triglycerides were elevated to 251 mg/dL, but his cholesterol was within a normal range. Abdominal CT demonstrated diffuse fatty infiltration of the liver, enlarged appendix suggestive of uncomplicated appendicitis, and a normal

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**Table 1. Summary of the Clinical and Laboratory Findings for the 3 SARS-CoV-2-Infected Children Presenting With Pancreatitis**

	Case 1	Case 2	Case 3
Race	Caucasian	Hispanic	Asian
BMI	34.4	29.5	18.7
Pulmonary symptoms	Nasal congestion	None reported	Cough
Extrapulmonary symptoms	Anosmia, ageusia, vomiting, and abdominal pain	Headache, chills, tactile fever, abdominal pain, hematochezia, and epistaxis	Subjective fever, nausea, and abdominal pain
Physical exam findings	Epigastric tenderness	Epigastric tenderness	Epigastric tenderness
WBC ( $4.19\text{--}9.43 \times 10^3/\text{uL}$ ) <sup>a</sup>	4.5	8.4	3.4
Percent lymphocytes (15.5%–56.6%) <sup>a</sup>	18.6	17.3	51.5
Absolute lymphocyte count ( $0.97\text{--}3.96 \times 10^3/\text{uL}$ ) <sup>a</sup>	0.85	1.46	1.74
CRP (0–0.5 mg/dL) <sup>a</sup>	1.47	24.11	Not performed
ESR (0–15 mm/h) <sup>a</sup>	4	99	Not performed
Serum Glucose (60–100 mg/dL) <sup>a</sup>	126	90	82
AST (14–35 U/L) <sup>a</sup> /ALT (9–24 U/L) <sup>a</sup>	53/86	47/54	15/9.6
Lipase (4–39 U/L) <sup>a</sup>	233	582	1909
Gastrointestinal findings on imaging	Mild stranding around the head of the pancreas	Fatty infiltration of the liver, enlarged appendix, and normal pancreas	Hepatomegaly, single gallstone, and prominence of the pancreas
Pulmonary findings on imaging	Scattered ground-glass opacities in bilateral lung fields	Interstitial opacities with peribronchial thickening	Not evaluated
SARS-CoV-2 RT-PCR	Positive	Positive	Positive

Abbreviations: BMI, body mass index; WBC, white blood cell; CRP, c-reactive protein; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ESR, sedimentation rate; RT-PCR, real-time reverse transcription-polymerase chain reaction.

<sup>a</sup>Numerical values within parentheses indicate the normal range for each laboratory test.

pancreas. Chest radiography noted central interstitial opacities with peribronchial thickening (See Table 1). He was diagnosed with appendicitis and pancreatitis and admitted to the hospital where he was made NPO (nothing by mouth) and started on intravenous fluids and piperacillin-tazobactam. Repeat laboratory studies demonstrated an increase of his amylase and lipase to 215 and 953 U/L, respectively. The diagnosis of COVID-19 was confirmed with a positive RT-PCR for SARS-CoV-2. With continued epigastric pain more concerning for pancreatitis rather than appendicitis, antibiotics were discontinued. His abdominal pain improved with the advancement of his diet, and he was discharged home on hospital day of 4 once tolerating a normal diet.

### CASE 3

A 16-year-old female with a history of pancreatitis over a year ago presented to the emergency department with nausea and epigastric abdominal pain radiating to her back for 3 days duration. She was unable to tolerate any food or liquids. She did report having subjective fever and a slight cough about a week prior to presentation and was found to be positive for SARS-CoV-2. On physical exam, she was hemodynamically stable with mild epigastric pain but without signs of respiratory distress. Pertinent laboratory findings include slight leukopenia to  $3.4 \times 10^3/\text{uL}$  with 51.5% lymphocytes, mild neutropenia to  $1.3 \times 10^3/\text{uL}$ , normal liver enzymes, an elevated lipase to 1909 U/L, and normal triglycerides and cholesterol. Repeat COVID testing was also positive. Her abdominal ultrasound

demonstrated mild hepatomegaly, a single gallstone, and prominence of the pancreatic head, tail, and duct (See Table 1). She was admitted and started on intravenous fluids, pain medications, and a clear liquid diet. Because of her previous history of pancreatitis, an evaluation for a possible genetic etiology was performed and was negative. As her symptoms improved, her diet was slowly advanced, and she was discharged on day 3 of hospitalization. She did not develop any respiratory symptoms during her hospitalization.

### DISCUSSION

The association of pancreatitis and COVID-19 infection has been suggested over the past several months with a few case reports, but there has only been 1 report of pancreatitis in a child to our knowledge. Unlike our patients, the 7-year old in the previous case report presented with necrotizing pancreatitis 2 weeks prior to her COVID-19 diagnosis [2]. Pancreatitis has been reported in several viral diseases, including mumps, measles, Epstein-Barr virus, hepatitis A and E, and Coxsackievirus [1, 3], thus making the association between SARS-CoV-2 and pancreatitis plausible. All 3 of our patients who were under the age of 16 developed symptoms about a week into their COVID-19 illness. Although the patient in case 1 did not have a SARS-CoV-2 test at the onset of his symptoms, the presence of anosmia and ageusia is highly suggestive of COVID-19. The proposed pathophysiology of the involvement of the pancreas by SARS-CoV-2 is because of the expression of angiotensin-converting enzyme 2 in both the islet cells and the exocrine

portions of the pancreas [4]. Pancreatic injury during an acute SARS-CoV-2 infection could also be secondary to an immune-mediated injury [3, 5]. Although it is difficult to rule out other possible etiologies for pancreatitis in the 3 patients presented in this report, especially since a complete medication history was not obtained, the timeline of diagnosis with COVID-19 and pancreatitis appears to have a temporal association. Thus, providers should consider SARS-CoV-2 in their differential diagnoses when managing patients with extrapulmonary symptoms including gastrointestinal symptoms.

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