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Case Report

Complicated Appendicitis in a Pediatric Patient with SARS-CoV-2 Infection: A Case Report

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Abstract

Background: Appendicitis is a common acute surgical condition in the pediatric population. With the rise of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), many efforts have been made to understand the association of this virus with other disease entities. However, the association of acute appendicitis and SARS-CoV-2 infection in children has not been well established. Few cases have been described in the literature with different hypotheses attempting to link the two entities. This highlights the need to be aware of such possible associations to achieve proper diagnosis and management and avoid complications.

Case Report: In this report, we describe the case of a seven-year-old boy who presented to our institution with uncomplicated appendicitis. The child was found to have SARS-CoV-2 infection on routine hospital testing. His condition deteriorated within hours, and he progressed from uncomplicated to complicated appendicitis. The child underwent surgical management followed by further medical management until he recovered. He had a smooth recovery and experienced no complications.

Conclusion: There is still no definite explanation concerning the effect of COVID-19 on appendicitis. Clinicians should be aware of the possibility of acute appendicitis in the context of pediatric SARS-CoV-2 infection and anticipate a possible progression of the disease course triggered by the virus.

Keywords: SARS-CoV-2, COVID-19, Acute Abdomen, Appendicitis, Pediatrics, Surgery, Case Report

Introduction

Appendicitis is one of the most common acute surgical conditions in children [1]. It affects up to 250,000 children per year, commonly occurring between 10 and 19 years of age [2]. The pathophysiology of appendicitis is linked to an obstruction of the appendiceal lumen that leads to impaired perfusion and consequently, ischemia and necrosis of the appendix [1]. The diagnosis of appendicitis is clinical, but imaging may be necessary to confirm the diagnosis. Computed Tomography (CT) scan is the modality of choice; however, the concern of radiation in children leads physicians to choose ultrasound as the preferred modality [2]. Appendicitis can be acute or chronic. Acute appendicitis presents as a sudden onset of pain associated with fever, anorexia, and vomiting [3]. Chronic appendicitis, on the other hand, is a long-standing inflammation that presents as prolonged or intermittent pain [3].

After the declaration of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) as a global pandemic by the World Health Organization (WHO) on March 11, 2020 [4], efforts have been made to understand the complications associated with this virus. Besides the respiratory signs and symptoms, gastrointestinal manifestations are also common. According to the Centers for Disease Control and Prevention (CDC), the incidence of SARS-CoV-2 in the pediatric population is unknown. This is due to the lack of widespread testing and the allocation of available resources to adults and patients with severe illness [5]. Thus far, SARS-CoV-2 has shown milder symptoms in children vs. adults [6]. These symptoms include cough and fever most commonly, in addition to other nonspecific symptoms such as rhinorrhea, myalgia, and headache. However, in rare cases, severe complications of this virus can arise in children [2]. These include Multisystem Inflammatory Syndrome in Children (MIS-C), myocarditis, and Kawasaki Disease [7, 8]. While gastrointestinal involvement is increasingly recognized among SARS-CoV-2 infected children, there is still limited data linking acute appendicitis to the latter. Reporting this observation is important as it will help further our understanding of the disease manifestations in the pediatric population. We hereby discuss the case of a 7-year-old boy who presented to the emergency department with an acute abdomen, tested positive for SARS-CoV-2, and was diagnosed with acute uncomplicated appendicitis that progressed rapidly to a complicated one.

Case Presentation

A seven-year-old boy presented to the Emergency Department (ED) with fever and abdominal pain of one-day duration. The family reported exposure to SARS-CoV-2 six days before presentation. After three days of exposure, the patient developed a fever of 38°C. This was followed by a right lower quadrant abdominal pain one day before presenting to our ED. The patient also had a febrile episode of 39.5°C, as well as one episode of non-bilious vomiting and multiple occurrences of non-mucoid, non-bloody diarrhea. There was no decrease in food intake or urine output and no upper respiratory tract symptoms. Physical examination revealed an irritable child with a tender abdomen and positive McBurney's and Rovsing's signs. His temperature was 36.8 °C, his heart rate was 114 bpm, and his oxygen saturation was 100%.

His blood tests revealed a white blood count of $6.49x10^3$/μL (normal range [NR] = $4.5\text{-}11x10^3$/μL), with 58% neutrophils (NR=35-70%), and an elevated C-reactive protein (CRP) level of 13 mg/dL (NR < 0.5 mg/dL). An ultrasound revealed an appendicolith measuring 8 mm and obstructing the appendix. The ultrasound findings aligned with a diagnosis of uncomplicated appendicitis (Figure 1). Molecular nucleic acid amplification test (NAAT) testing through a nasopharyngeal swab was positive for SARS-CoV-2. Urinalysis revealed microhematuria.

The child was admitted to the hospital and started on:

- Intravenous (IV) hydration with 5% dextrose and 0.45% NaCl solution
- IV paracetamol as needed
- IV antibiotics: ceftriaxone 75mg/Kg/day divided every 12 hours, and metronidazole 40mg/Kg/day divided every 8 hours, in preparation for an appendectomy.

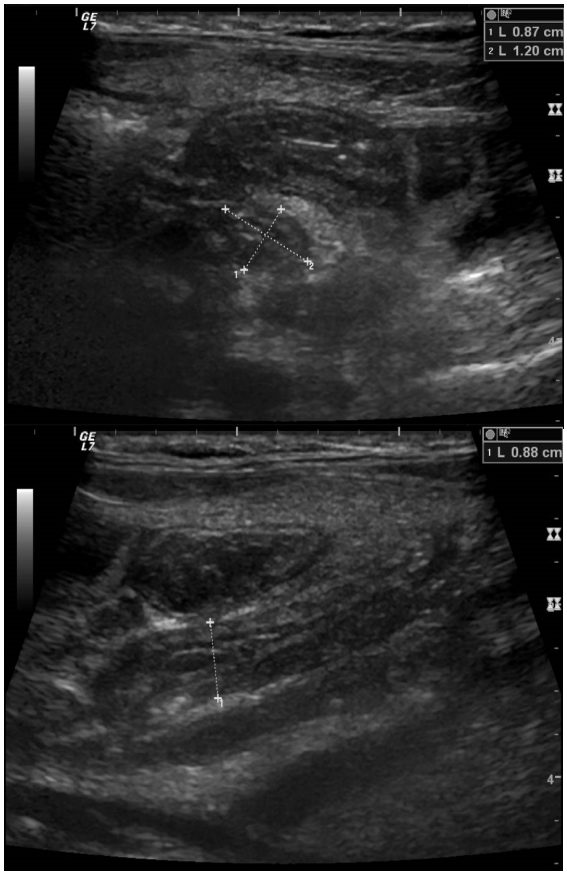

Figure 1: *Initial radiologic findings suggestive of uncomplicated appendicitis. An enlarged appendix in a subcecal location showing a posteriorly ascending configuration can be visualized; it shows a thick wall, reaching a diameter of 9mm, containing minimal amount of intraluminal fluid at its tip with associated appendicolith measuring 8mm.*

Within hours, the child had worsening pain and seven episodes of non-bloody, non-mucoid diarrhea. He developed a fever of 38.6 °C, and his abdomen became profusely tender and diffusely rigid. The child underwent an open appendectomy 17 hours post-admission, revealing a friable appendix with false membranes. Pathology demonstrated an acute necrotic suppurative appendicitis with peri-appendicitis.

Post-operatively, IV hydration was increased. The patient was stable. Physical examination revealed oozing on the wound dressing, so a culture was performed, and 135 mg of amikacin was added every 8 hours to the treatment regimen. The culture revealed the presence of *Pseudomonas aeruginosa*. The child's vitals were monitored until the fever subsided. The surgical site was monitored for any signs of infection, the dressing was changed by the surgery team as needed and the child was also monitored through markers of inflammation such as white blood cell count and CRP. No treatment was administered targeting the SARS-CoV-2 infection. SARS-CoV-2 Polymerase Chain Reaction (PCR) test on day seven post-operation was negative. The patient was discharged on ciprofloxacin 250 mg every 12 hours and metronidazole 250 mg every 8 hours to complete a 14-day course on both antibiotics. The patient's parents followed up with the child's pediatrician, and no further complications occurred.

Discussion

In this article, we highlighted the case of a patient with SARS-CoV-2 infection along with acute appendicitis. The patient had radiologic findings of uncomplicated appendicitis seventeen hours before surgery. The patient rapidly progressed into ruptured appendicitis with a pelvic abscess and false membranes. Our question was: Could this rapid progression be linked to SARS-CoV-2?

Few reports have described cases of acute appendicitis in the setting of COVID-19 [6, 9, 10]. A publication from South Africa reported four children with acute appendicitis and concomitant COVID-19 [9]. Of the four cases, three were diagnosed with MIS-C, while the remaining patient was diagnosed with COVID-19 after being tested due to the hospital's screening policy [9]. Another publication from New Jersey reported that 10 out of 48 children with confirmed SARS-CoV-2 infection were later diagnosed with appendicitis. They suggested a possible

pathophysiological link between SARS-CoV-2 and acute appendicitis. Moreover, a publication from Morgan Stanley Children's Hospital (MSCH) in New York during the peak of COVID-19 revealed a correlation between the year of the pandemic and the following characteristics of acute appendicitis: delayed presentation, more severe disease course, and worse outcome [11].

Data suggests that the virus could be secreted from infected enterocytes of the gastrointestinal (GI) tract [12]. One possible explanation for this is supported by the highly expressed angiotensin-converting enzyme 2 (ACE2) by enterocytes [12]. ACE2 receptors are thought to be the host receptors for viral entry of SARS-CoV-2 into the cells [12]. Although ACE2 is expressed by the glandular cells of the appendix, SARS-CoV-2 was not detected in formalin-fixed, paraffin-embedded tissue when tested in our patient's appendiceal sample. This finding is in line with another publication by Meyer et *al.*, where SARS-CoV-2 was not detected from appendiceal samples retrieved from 2 pediatric patients [6]. SARS-CoV-2 can also possibly induce lymphoid follicular hyperplasia of the epithelial lining of the appendix leading to luminal obstruction, inflammation, and ischemia [12]. This might explain the rapid exacerbation and progression to complicated appendicitis, which was seen in the case of our patient.

To date, there has been limited data in the literature highlighting a possible correlation between appendicitis and SARS-CoV-2. Published data report a statistically significant increased rate of appendiceal perforation during the pandemic [13]. Most of the publications attribute the transition of uncomplicated appendicitis to complicated appendicitis to the delay in treatment [14]. The delay itself has been attributed to parental doubts about hospital safety and concerns regarding contracting the virus [14]. However, another study refuted this assumption when comparing SARS-CoV-2 positive patients with appendicitis and SARS-CoV-2 negative patients with appendicitis [10]. The authors reported that the overall rupture rate in positive patients (50%) was higher than that of negative patients (36.1%) and was not attributed to a delay in seeking healthcare, but to an exaggerated inflammatory response in positive patients that might play a role and lead to appendiceal rupture [10]. On the other hand, a retrospective study conducted in Spain refuted most of the claims and concluded that the pandemic did not increase the incidence of complicated appendicitis, nor did it lead to worse outcomes [15]. It also deduced that there was no parental delay or failure of early diagnosis by the medical team [15].

Our patient was managed with an open laparotomy and antibiotics. The management of complicated acute appendicitis is still controversial. Operative laparotomy or laparoscopy is advised for the management of complicated acute appendicitis without abscess, while non-operative management is advised for complicated acute appendicitis with abscess [16]. Many healthcare centers universally had to adjust the delivery of services in response to the pandemic with some only permitting emergency surgical procedures. While healthcare centers might opt for the non-operative management of complicated appendicitis in hopes of decreasing transmission to healthcare providers, Bonadio et *al.* report a greater length of hospital stay in children with perforated appendicitis who are managed non operatively, which justifies the preference for an open laparotomy over medical treatment during the pandemic [17]. This decreases the hospital staff's risk of exposure and is more cost-effective both to the hospital and the patient.

Our patient suffered from a wound infection post-operatively; however, it is important to note other possible complications of appendicitis that can develop in the pediatric population. These complications are mainly due to the infectious nature of the disease that might lead to sepsis or even septic shock in

advanced appendicitis [18]. Wound complication is the most common complication post-appendectomy; however, it is less common in the pediatric population than in adults [18]. Moreover, around 20% of children with perforated appendicitis will develop a postoperative abscess, while only 0.8% of patients develop an abscess among patients without perforation [11].

Conclusion

A variety of complications have been attributed to SARS-CoV-2 infections. So far, there is still no clear evidence whether complicated appendicitis may be the result of direct infection of the SARS-CoV-2 virus targeting appendiceal tissues or if it is the result of an exaggerated immune response in COVID-19 positive patients or even due to the delay in diagnosis and management attributed to the ongoing pandemic. Although there is no evidence yet for the need to alter the management, clinicians should be aware of the possibility of acute appendicitis in the context of pediatric SARS-CoV-2 infection and anticipate a possible progression of the disease course triggered by the virus. For this reason, clinical and surgical approaches should not be delayed when clinically indicated.

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