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CASE REPORT

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Acute appendicitis during the clinical course of COVID-19 in a 13-year-old boy: Complication or coincidental?

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Abstract

Gastrointestinal symptoms appear to be one of the most common presentations of SARS-CoV-2 infection, later named COVID-19. The symptoms such as nausea, emesis, abdominal pain, and diarrhoea may be recognised as either a finding of COVID-19 or prominent presentation of multi-inflammatory syndrome in children (MIS-C). COVID-19 may present with acute appendicitis and/or may mimic its clinical findings. Although, coexistence of acute appendicitis and COVID-19 has been well documented, it is not clear whether appendicitis is a complication of COVID-19 or coincidence in children. A 13-year-old boy who developed acute appendicitis during the clinical course of COVID-19 is presented to discuss the possibility of causal relationship between appendicitis and COVID-19 in children.

1 | INTRODUCTION

The COVID-19 outbreak, which first appeared in Wuhan, China, at the end of December 2019, soon affected the whole world.[1] It has been observed that children have milder clinical signs of the virus than adults and sometimes act as asymptomatic carriers of infection.[2] The gastrointestinal symptoms are one of the most common presentations of COVID-19 and the prevalence has reached as high as 92% in children in some reports.[3] Gastrointestinal manifestation of COVID-19 may mimic and/or cause acute abdominal findings including appendicitis, intussusception, gastrointestinal bleeding, and pneumatosis intestinalis.[4–7] Primary symptoms such as fever and abdominal pain in paediatric patients with COVID-19 can be confused with appendicitis or, conversely, a true appendicitis may go unnoticed due to these symptoms.

It has been suggested that acute appendicitis (AA) may occur as a complication of COVID-19.[8] There are several possibilities that COVID-19 may cause AA. Firstly, SAR-CoV-2 may induce lymphoid follicular hyperplasia of the epithelium lining of the appendix and may lead to lumen obstruction, inflammation and ischaemia.[9] Secondly, angiotensin converting enzyme-2 (ACE2) receptor is functional receptor of COVID-19 and is also expressed in gut microbiome including the glandular cells of the appendix.[10] Therefore, the gastrointestinal route is also considered as an entry site for the virus. SARS-CoV-2 virus can be secreted form infected enterocytes and can be isolated in faecal swabs several weeks after nasal swabs become negative. Meyer et al. first draw attention the possible association of AA and COVID-19 in four children.[9] However, it is not clear whether the occurrence of AA is complication of COVID-19 or it is a coincidental finding. Herein, we report a 13-year-old boy who developed AA during the clinical course of COVID-19 to discuss whether the relationship between acute appendicitis and COVID-19 is causal or coincidental.

2 | CASE REPORT

A 13-year-old boy admitted to the emergency department with fever, abdominal pain, vomiting and diarrhoea. On admission, his body temperature was 39.3°C, respiratory rate was 20/min, heart rate was 90/bpm and blood pressure was 90/60 mmHg. In his family history, his father complained about coughing 10 days ago but his polymerase-chain-reaction (PCR) test for SARS-CoV-2 was negative. However, chest computed tomography (CT) scan of the father was suggestive for COVID-19 pneumonia.

The physical examination of the patient revealed minimal abdominal tenderness at all quadrants. Laboratory findings including total blood counts showed haemoglobin level of 16.3 gr/dL, white blood cells 9.3×10^3 /μL, lymphocytes 0.98×10^3 /μL. The biochemical tests including serum electrolytes, liver and renal function tests were

within normal limits. The C-reactive protein was also 19.73 mg/dL (normal range; 0–0.5 mg/dL). The SARS-CoV-2 PCR test of nasopharyngeal swab was found positive. Abdominal sonography did not reveal radiological findings of AA. Magnetic resonance imaging (MRI) of the abdomen showed no evidence of inflammation of the appendix (Figure 1). The patient was diagnosed as COVID-19 with gastrointestinal involvement and hospitalized to an isolated infection service for treatment of COVID-19 disease. Intravenous fluid treatment and antibiotics including Ciprofloxacin (20 mg/kg/day) and Favipiravir (initial dose was 1200 mg, followed by another 1200 mg at the eighth hour and 800 mg at the 16th hour. On the second to fourth days, 800 mg every 12 h was administered) were started. The patient had persistent fever despite the antibiotics. The chest x-ray was normal and there were no signs of COVID-19 pneumonia. Three days after the hospitalisation, the patient did not tolerate oral feedings. The complaints including diarrhoea and abdominal pain progressed and physical examination revealed remarkable tenderness on both quadrants with guarding and rebound. At the third day of hospitalisation, the level of white blood cells was 8.1×10^3 /μL and C-reactive protein (CRP) was 13.7 mg/dL. Since, we could not evaluate faecal swabs for Covid-19 at that period of the pandemic, we repeated nasal swab test and found positive at the third day of follow-up. Then, abdominal CT examination was performed. CT scan showed inflamed appendix (10 mm in diameter) and inflammatory changes of the adjacent mesentery (Figure 2). The patient was diagnosed as AA due to COVID-19 and underwent urgent laparotomy. In surgical exploration, hyperaemia and inflammation of the appendix was evident and appendectomy was performed. The histopathology of appendix revealed obstructed lumen with microscopic evidence of acute inflammation. The patient was discharged form hospital 6 days after the appendectomy and the nasal swab test for Covid-19 became negative 2 days after discharge.

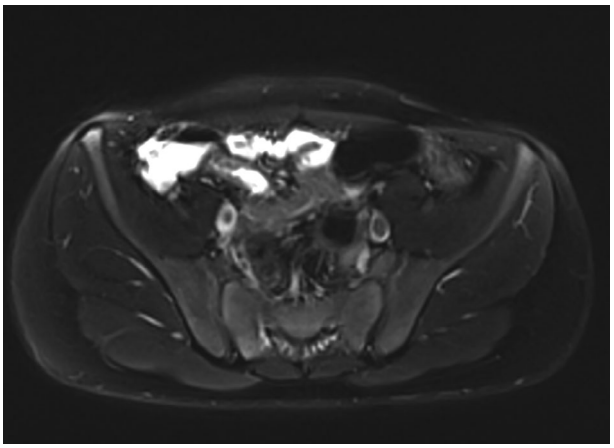

FIGURE 1 Axial T2-weighted fat saturated magnetic resonance image demonstrates normal terminal ileum and cecum. There is no evidence of inflammation of appendix

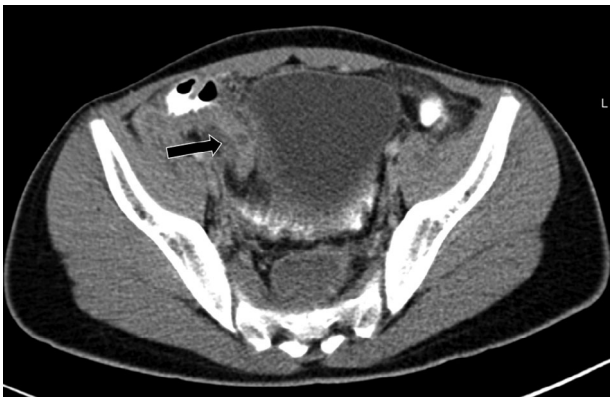

FIGURE 2 Axial contrast enhanced computed tomography scan shows dilated, tubular appendix (arrow) and periappendiceal soft tissue stranding

3 | DISCUSSION

Children with COVID-19 may present with clinical features of appendicitis as part of the multisystem inflammatory syndrome (MIS-C).[8–11] Meyer et al reported coexistence of COVID-19 infection and AA in four children.[9] In the previous reports, patients were diagnosed as AA and COVID-19 on admission. Therefore, controversy still exists regarding the causal relationship between AA and COVID-19. In our patient, we first demonstrate that AA developed during the clinical course of COVID-19 infection. The physical examination and abdominal imaging of the patient were not typical for AA initially. However, the gastrointestinal manifestations of COVID-19 were predominant on admission. Although, abdominal MRI was not suggestive for AA at initial evaluation, control abdominal CT scans at the third day of COVID-19 infection was demonstrative for appendicitis. Therefore, we suggest that relation between AA and COVID-19 may be causative rather than coincidental for this patient.

The general cause of appendicitis is obstruction of the lumen of the appendix by faecolith or hyperplasic lymphoid follicle. The cause of appendicitis in patients with COVID-19 has been shown to be viral entry through ACE2 receptors, which are abundant in the terminal ileum, and associated with terminal ileitis.[12,13] In the current case, the patient was diagnosed as AA without clinical features of MIS-C due to COVID-19. Also, the absence of faecolith in the lumen of the appendix suggests that obstruction of the appendix lumen with lymphoid hyperplasia may be the possible cause for AA. Malhotra et al. suggest that appendicitis is another postinfectious hyperinflammatory complication of SARS-CoV-2 and inflammation induce development of lumen obstruction and AA.[4] In the same report, the complicated appendicitis rate was 36% in negative SARS-CoV-2 patients but 50% in children with positive PCR tests.[4] This finding can be explained by either difficulties in diagnosis or late admission of patients during the pandemic. However, there is no evidence that COVID-19 may cause higher incidence of perforated appendicitis.

Since the clinical findings of AA overlaps with the symptoms of COVID-19, cross-sectional imaging methods are recommended for the patients with gastrointestinal findings. Terminal ileitis is a common finding and can be documented in patients with COVID-19 related

AA.[11] Previous reports suggest that AA can be subsequently ruled out by the use of abdominal CT scans.[8] The physical examination may not be distinctive for AA in patients with COVID-19 as well as MIS-C cases and repeated imaging can be required, as in our patient. Therefore, further evaluation with repeated imaging findings are needed to diagnose an AA in children with Covid-19.

Traditionally, appendectomy has been accepted as the standard treatment for appendicitis. The non-surgical treatment of appendicitis in a child with a concomitant COVID-19 infection has been reported.[14] However, there is no randomised clinical trial that demonstrates non-operative management of appendicitis is superior to appendectomy in patients with COVID-19. Moreover, previous studies report favourable postoperative outcomes after appendectomy in children with concomitant COVID-19 infection.[4,9] Sepsis was documented in only one immunocompromised patient after appendectomy.[9] Terminal ileitis without the signs of AA should require medical treatment and unnecessary surgical exploration should be avoided. Therefore, physicians should be kept in mind that AA may develop during clinical course of COVID-19.

4 | CONCLUSION

Acute appendicitis can be also considered as a complication of COVID-19 and may develop during the clinical course of COVID-19. Children with gastrointestinal manifestation of COVID-19 should be closely followed up for possible development of appendicitis and further investigation with repeated physical examination are needed. A timely imaging of abdomen has a critical role in the diagnosis of AA in children during pandemics and can be repeated according to the changes in clinical findings.

CONFLICT OF INTEREST

All authors declare no conflict of interest.

INFORMED CONSENT

A written informed consent was obtained from patient and caregivers.

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