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Ruptured Appendicitis and Covid-19 related Multisystem Inflammatory Syndrome (MIS-C) in a Child

Rawan Alhalabi *[1], Dalia Belsha [2], Basil Nasrallah [3], Qusai Mashlah [4], Proff. Omendra Naryan [5], Muhammad Eyad Ba'ath [6]

1. Trainee Pediatrician - American Hospital Dubai, Dubai, UAE.

2. Consultant Pediatric Gastroenterologist - American Hospital Dubai, Dubai, UAE.

3. Consultant Pediatrician - American Hospital Dubai, Dubai, UAE.

4. Pediatric Surgeon - Damascus University, Syria, Damascus.

5. Consultant Respiratory Pediatrician - American Hospital Dubai, Dubai, UAE.

6. Consultant Pediatric Surgeon & Urologist - American Hospital Dubai, Dubai, UAE.

Corresponding Author: Rawan Alhalabi, Trainee Pediatrician - American Hospital Dubai, Dubai, UAE.

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Abstract

Multisystem Inflammatory Syndrome in Children (MIS-C) is an uncommon but serious disease that usually manifests around four weeks after Covid-19 infection. It involves an inflammatory reaction in more than 2 organs, high fever, and elevated inflammatory markers. MIS-C and appendicitis can present with acute abdomen, which represents a diagnostic and therapeutic pitfall. Here we present a previously healthy 9-year-old female, who initially had the working diagnosis of possible Covid-19 related MIS-C. She improved with treatment for MIS-C, but later presented with ruptured appendicitis and abscess formation and had a laparotomy. The child recovered fully after a protracted hospital course. Three-dimensional imaging of the abdomen in the form of an ultrasound scan or a computerized tomography should be applied early while managing MIS-C. Our case raises the possibility that MIS-C can lead to appendicitis and here we discuss the potential pathophysiology explaining this.

Keywords*: Covid-19; Appendicitis; Acute abdomen; Multisystem Inflammatory Syndrome in Children MIS-C; Pediatric Inflammatory Multisystem Syndrome PIMS.*

Introduction

Coronavirus disease-2019 (Covid-19), first detected in 2019, became a worldwide pandemic in 2020 and is caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV2) virus. Covid-19 symptoms in the pediatric age group are mostly mild. MIS-C is an uncommon but serious disease that usually manifests around four weeks after Covid-19 infection. By definition, it involves an inflammatory reaction in more than 2 organs, high fever, and elevated inflammatory markers[1]. Clinical and laboratory features of MIS-C are similar to those of Kawasaki disease, Kawasaki disease shock syndrome, and toxic shock syndrome[2]. Moreover, MIS-C and appendicitis can present with acute abdomen, and since the treatment is very different, this represents a diagnostic and therapeutic pitfall.

Case Presentation

A previously healthy 9 years old female, presented to the emergency department of another hospital with a one-day history of fever (38ºC), headache, general malaise, mild generalized abdominal pain, and dry cough. On examination, she had rebound tenderness in the right iliac fossa. Her CRP was elevated. Covid-19 RT-PCR test was positive. The child was given one dose of ceftriaxone and sent home. A week later, she presented again with non-bilious vomiting, watery diarrhea, moderate generalized abdominal pain, and dry cough. Physical examination was within normal. Her laboratory work-up during the second presentation is shown in Table I. Echocardiography and ECG were normal.

Blood test	Result	Reference range
Troponin_1	↑ 0.26 ng\ml	0.025 – 0.06
CRP	↑ 155 mg\L	0.02 – 14.4
ESR	↑ 80 mm\hr.	≤20
Procalcitonin	↑ 0.65 ng\ml	0.01 – 0.49
Ferritin	↑ 275 ng\ml	7 – 140
LDH	↑ 334 U\L	60 – 170
D-dimer	↑ 3.39 µ\ml	0.4 - 2.27

Table I, laboratory work-up

A working diagnosis of MIS-C syndrome was presumed, and she was admitted for close monitoring and started on the following treatment protocol:

- IVIGg; 2gm\kg infusion over 10 hours.
- IV methylprednisolone 1mg\kg\day BID.
- Aspirin 75mg per oral 2 taps once daily.
- Ondansetron HCL 4 mg BID.

During hospitalization (5 days), she improved and became asymptomatic. Inflammatory markers gradually declined. She was then discharged on a weaning regime of oral prednisolone over 10 days. A week later, she presented with fever, rigors, anorexia, severe right lower quadrant (RLQ) pain, vomiting, and diarrhea. On abdominal examination, she had right iliac fossa tenderness and percussion tenderness. Her bloods were notable for elevated WBC 19.9 (reference; 5 – 15 *10^9) and neutrophilia 15.8 (reference; 2 – 8 #). PCR was negative for Covid-19. CT abdomen with contrast showed RLQ abscess with fecalith, likely in keeping with ruptured appendicitis. Figure I & Figure II

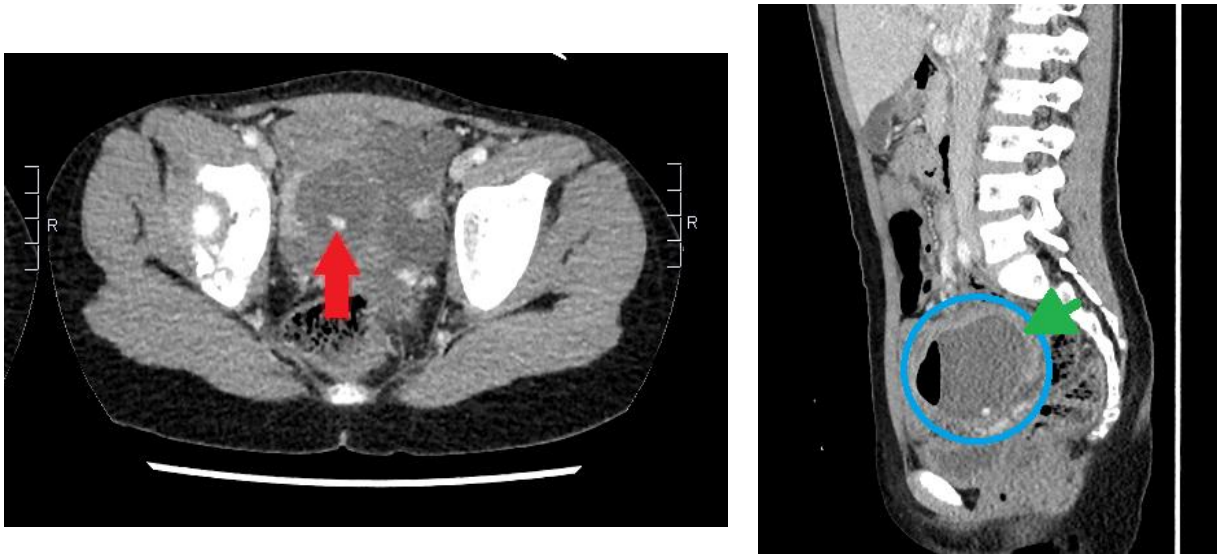

Figure I - Figure II, CT scan with contrast reveals abdominal-pelvic abscess with air-fluid level (circle), abscess wall hyperenhancement (green arrowhead), and appendicolith (red arrow).

She initially had percutaneous drainage of the abscess and intravenous antibiotics. This failed to improve her clinical and biochemical condition and therefore she underwent a laparotomy, appendectomy, drainage of abscess, and placement of multiple abdominal drains. The pus from the abscess was cultured which showed a mixed growth of aerobes and anaerobes. Accordingly, she received broad-spectrum antibiotics.

Following the operation, she improved gradually and was discharged home after ten days. She was subsequently reviewed in the clinic and a complete resolution of her symptoms and laboratory abnormalities was noted.

Discussion

Covid-19 symptoms are variable. In adults, the infection can be asymptomatic, while the majority of cases have mild symptoms[3], and nearly 11% have at least one GI symptom[4]. The majority have a good prognosis, and the disease can rarely be severe or fatal[5]. In children, nearly half are asymptomatic, and the other half mostly have mild symptoms[6]. The symptoms are similar to a viral upper respiratory tract infection: dry cough (the most common symptom affecting 48% of symptomatic children), sore throat, sneezing as well as rhinorrhea and nasal congestion[3]. Fever is the second most common symptom in covid positive symptomatic children (47-51%)[3, 7]. According to the American Academy of Pediatrics (AAP), every persistent fever must be evaluated for the rare Covid-19

complication known as Multisystem Inflammatory Syndrome in Children (MIS-C), or Pediatric Inflammatory Multisystem Syndrome (PIMS)[8]. MIS-C is an inflammatory condition defined by the following diagnostic criteria as shown in Table II [2,3,8,9,10,11,12].

• ***Fever*** ≥ 38ºC for 24 hours or more in a patient less than 21 years old
• Elevated ***inflammatory markers*** including (but not limited to) one or more: ○ Erythrocyte Sedimentation Rate (ESR) ○ C-Reactive Protein (CRP) ○ Fibrinogen ○ Procalcitonin ○ D-dimer ○ Ferritin ○ Lactic Acid Dehydrogenase (LDH) ○ Interleukin 6 (IL-6) ○ Elevated neutrophils, reduced lymphocytes ○ Low albumin
• **Inflammatory reaction in more than 2 organs**, including but not limited to: ○ Gastrointestinal symptoms (70%); diarrhea, abdominal pain, nausea, and vomiting. ○ Kawasaki disease-like (partially); rash (57%), conjunctivitis, mucosal changes, and red or swollen hands and feet. ○ Coronary artery dilation or aneurysms (6-24%) and arrhythmias (7-60%). ○ Acute kidney injury ○ Respiratory symptoms ○ Hemodynamic instability +\- shock ○ Congestive heart failure or pulmonary embolism
• Positive (RT-PCR or serology) or suspected current or recent SARS-2 infection within the last 4 weeks prior to the onset of symptoms. However, it seems to develop after the infection rather than during the acute stage of COVID-19
• No conceivable other diagnoses

Table II, Diagnostic criteria for MIS-C

While the clinical presentation of appendicitis and COVID19 related MIS-C may overlap, two potential scenarios might explain our case:

First: COVID-19 infection's usual presentation incidentally combined with acute appendicitis; with or without MIS-C. Both COVID-19 infection and acute appendicitis are common conditions, and it is plausible that they may concurrently occur in the same patient. Ruptured appendicitis can explain the clinical picture and lab results, except for troponin 1. The patient might have had acute appendicitis

from the very beginning. The diagnosis of appendicitis might have simply been delayed due to the concurrent diagnosis of MIS-C. A trend towards a delayed diagnosis of appendicitis has been well documented during the pandemic, An Australian study showed a marked increase in the numbers of complicated appendicitis during the COVID-19 period; 60.5% compared to 30.4% before the pandemic[13]. This might be due to delayed presentation due to public fears of attending hospitals and medical centers during the pandemic, as well as health system overload.

The clinical overlap in the presentation might have led to the need for increased use of CT to diagnose appendicitis during the pandemic, as demonstrated in a retrospective observational study that showed 45.5% of appendicitis cases were diagnosed with CT as compared to 29.8% before the pandemic[14].

Second: COVID-19 infection complicated by MIS-C which in turn evolved as appendicitis. Multiple studies proposed a connection between COVID-19 and appendicitis[15, 16].

Since MIS-C is a multi-organ inflammatory reaction to SARS-2, the appendix might be one of the organs included in this inflammatory storm. SARS-2 attaches to ACE2 (Angiotensin Converting Enzyme 2) receptors, which are expressed in multiple organs including intestinal mucosa cell membrane[5].

Thus, the appendix could be inflamed in the context of MIS-C. Our case fits the criteria required for an MIS-C diagnosis, which supports this scenario. This is further supported by the elevated cardiac enzymes, and the improvement in symptoms during the first hospital stay where the treatment was directed towards MIS-C.

Conclusion

Given the clinical and therapeutic overlap between acute appendicitis, COVID-19 infection, and MIS-C, it is imperative three-dimensional imaging of the abdomen in the form of an ultrasound scan or computerized tomography is applied early in the course of managing possible MIS-C to avoid delay in diagnosis and treatment. There might be a possibility that MIS-C could lead to appendicitis. This possibility requires further reporting of such cases to be confirmed and elucidated.

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