

Case Report

COVID-19 Multisystem Inflammatory Syndrome in Children (MIS-C) simulating as acute appendicitis: A case report

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ABSTRACT

Background: As the COVID-19 pandemic continues to disrupt global affairs through a variety of manifestations, a severe presentation of some COVID-19 pediatric patients has emerged, presenting as multisystem inflammatory syndrome in children (MIS-C) that may mimic surgical conditions.

Case Presentation: We report the case of a 9-year-old boy who presented with acute, intermittent abdominal pain and fever. Further inquiry suggested a hyper inflammatory disorder affecting multiple organ systems. Upon COVID-19 PCR testing, the patient was reported as COVID-19 positive in the second test on the 2nd day of admission, after an initial negative test upon admission. We describe the course of this patient's disease from presentation until discharge and discuss the emerging literature on this potentially fatal complication.

Conclusion: MIS-C should be a differential diagnosis in patients who may present with acute abdominal pain in the emergency room.

Keywords: COVID-19, SARS-CoV-2, Multisystem Inflammatory Syndrome in Children (MIS-C), Kawasaki Disease.

INTRODUCTION

Respiratory Syndrome Corona virus 2 (SARS-CoV-2) has the potential to infect all age groups, however, children rarely contract it and usually present with milder symptoms or remain asymptomatic.[1,2] Although respiratory symptoms are typically present in COVID-19, this disease should not be ruled out in the absence of these symptoms. Specifically, gastrointestinal symptoms are emerging as potentially the only presenting complaint in some pediatric cases.

According to a multicenter, cross-sectional study, up to 48.5% of patients experience gastrointestinal symptoms such as nausea, vomiting, diarrhea and abdominal pain, whilst 3% of adults presented with gastrointestinal symptoms without the presence of respiratory symptoms. Comparatively, 10% of children presented

with only gastrointestinal symptoms. Diarrhea was the most common gastrointestinal symptom in both children and adults, whilst vomiting was much more common in children than adults. Furthermore, it was noted that patients with digestive symptoms were more likely to have poorer prognosis compared to those who had no digestive symptoms.[3]

Recently, concern has developed for MIS-C with gastrointestinal symptoms in the context of COVID-19.[4] A case series of 8 patients recently highlighted SARS-CoV-2 positive pediatric patients primarily presenting with fever and abdominal pain, which could be mistaken for appendicitis.[5] In this case report, we document a child whose presentation was suspicious for appendicitis. However, upon further investigation, the patient was discovered to be SARS-CoV-2 positive and with evidence of MIS-C.

CASE REPORT

An 8-year-old boy presented to the emergency department with sudden onset and intermittent abdominal pain, and fever for a week. The pain began in the periumbilical region, before migrating to the right iliac fossa. It was associated with nausea and 1-2 episodes of vomiting per day, which was clear and non-bilious. No diarrhea, constipation or any other gastrointestinal symptoms were noted in the history. He also experienced intermittent high-grade fever for a week. He also developed burning sensation in his mouth and eyes with watery discharge. Rest of his review of systems was unremarkable.

Owing to the current COVID-19 pandemic, a thorough history for exposure was taken. Importantly, no one in the family had contracted COVID-19 and there was no recent history of travel. Furthermore, he did not have any history of respiratory symptoms. However, prior to presenting at the emergency department, he had visited a local hospital, where routine tests such as LFTs and CBC ordered and returned normal, and he was sent home on supportive treatment. The child was otherwise healthy, vaccinated according to the Extended Program for Immunization (EPI) protocol, and had no significant past surgical history.

On physical examination in the emergency room, he appeared to be a pale, irritable child. He was tachycardic (122 bpm), hypotensive (98/59 mmHg), febrile (39.5°C), with a respiratory rate of 22 and an oxygen saturation of 99%. His abdominal examination demonstrated marked guarding, with positive rebound tenderness and Rovsing sign in the right iliac fossa. However, psoas and obturator signs were negative. No mass was palpated in the abdomen. Furthermore, his oral mucosa appeared inflamed and erythematous and there was watery discharge from his eyes. The rest of his physical examination was unremarkable.

The child was found to have neutrophilia (90.7%) with a total leucocyte count of $6.3 \times 10^9/L$. Hyponatremia (128 mmol/L), hypokalemia (3.2 mmol/L) and hypochloremia (91 mmol/L) were also noted. At presentation, procalcitonin was normal, however C-reactive protein (CRP) was raised (151.77 mg/L) which is done routinely in children with infectious presentation. As per hospital policy, a COVID-19 PCR test was also conducted, which was negative. Blood cultures, stool cultures, Dengue IgM and Malarial peripheral smear returned negative as well. Clinically the child seemed to have acute appendicitis. An ultrasound abdomen did not suggest acute appendicitis but did note free fluid in the pelvis and Morrison's pouch. A subsequent Focused Abdominal CT (FACT) revealed a normal retrocecal appendix; however it did note significantly enlarged mesenteric lymph nodes with associated surrounding minimal fat stranding. The largest lymph node was detected in the right lower

quadrant, measuring 23 mm in the short axis. There was minimal thickening of the ileocecal wall (Fig. 1).

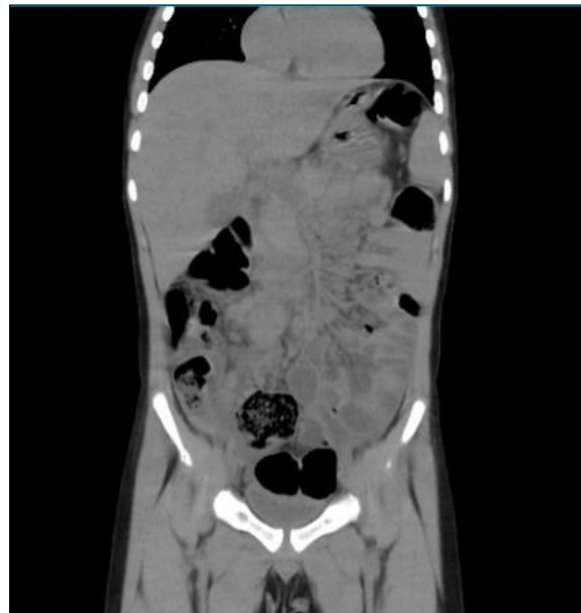


Figure 1: Significantly enlarged mesenteric lymph nodes can be visualized, the largest being in the right lower quadrant, measuring 23 mm in the short axis. There is minimal thickening of the ileocecal wall

The patient was resuscitated in the emergency room and admitted with the suspicion of acute appendicitis. However, given the associated conjunctivitis and mucositis of oral cavity, we started the child on broad spectrum intravenous antibiotics and observed him. The CT scan findings confirmed that the tenderness in the right iliac fossa was in fact an inflamed lymph node mimicking acute appendicitis. Over the next two days, the patient developed watery diarrhea, with no resolution in fever. A second COVID-19 PCR was then ordered on the 2nd day of admission on suspicion of this being a manifestation of COVID-19, which returned positive. Owing to emerging literature based on the preliminary results of various randomized controlled trials, it has been proposed that the potent anti-inflammatory effects of corticosteroids might prevent or mitigate the inflammatory response in some COVID-19, thereby dexamethasone was also administered.

The CRP remained elevated but had decreased to 51.92 mg/L by the 5th day of admission. Due to the improvement in clinical status, the patient was discharged on the 7th day of admission. The parents were advised to follow isolation protocols and return immediately upon the development of further symptoms or deterioration. Two weeks after discharge, the child is well, and asymptomatic.

DISCUSSION

MIS-C can involve the heart, lungs, kidneys, brain, skin, eyes and gastrointestinal organs. Recent reports

from Europe and North America have shed light on MIS-C as a potentially fatal complication of COVID-19 in children. Typically, these children tend to have a severe course of illness, often requiring admission to the intensive care unit. It has been noted that, in the context of positive COVID-19 serology, this pathologic process shares some features of Kawasaki disease, toxic shock syndrome, bacterial sepsis and macrophage activation syndrome.[6] As knowledge on it evolves, the Centre for Disease Control (CDC)[7] and World Health Organization (WHO)[8] have released preliminary case definitions, a comparison of which is made in Table 1. Our case fits in both the definitions of the CDC and WHO for MIS-C.

As the number of published case series on this condition increases, it has been noted that many patients have fever and mucocutaneous symptoms like those of Kawasaki's disease. Furthermore, it has long been suspected that viral illnesses tend to precede the symptoms of Kawasaki disease.[9] However, as opposed to Kawasaki disease, MIS-C tends to affect an older patient population (adolescents and children >5 years of age) and presents more frequently with cardiovascular manifestations.[4,10]

Table 1: A comparison of the CDC and WHO preliminary case definitions for MIS-C in COVID-19

CDC	WHO
<ol style="list-style-type: none"> Age <21 years presenting with fever ($>38.0^{\circ}\text{C}$ for ≥ 24 hours or subjective fever lasting ≥ 24 hours), laboratory evidence of inflammation (one or more of: elevated CRP, ESR, fibrinogen, procalcitonin, d-dimer, ferritin, LDH, IL-6, elevated neutrophils, reduced lymphocytes and low albumin), and evidence of clinically severe illness requiring hospitalization, with multisystem (>2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological); <p>AND</p> <ol style="list-style-type: none"> No alternative plausible diagnoses <p>AND</p> <ol style="list-style-type: none"> Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or COVID-19 exposure within the 4 weeks prior to the onset of symptoms 	<ol style="list-style-type: none"> Age 0–19 years of age with fever >3 days <p>AND two of the following:</p> <ul style="list-style-type: none"> Rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammation signs (oral, hands or feet). Hypotension or shock. Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponin/NT-proBNP), Evidence of coagulopathy (by PT, PTT, elevated d-Dimers). Acute gastrointestinal problems (diarrhea, vomiting, or abdominal pain). <p>AND</p> <ol style="list-style-type: none"> Elevated markers of inflammation such as ESR, CRP, or procalcitonin. <p>AND</p> <ol style="list-style-type: none"> No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes. <p>AND</p> <ol style="list-style-type: none"> Evidence of COVID-19 (RT-PCR, antigen test or serology positive), or likely contact with patients with COVID-19.

A recent large-scale study by Feldstein et al. reported the clinical manifestations of MIS-C in COVID-19. The gastrointestinal system was most commonly affected (92%), followed by the cardiovascular (80%), hematologic (76%), mucocutaneous (74%), and respiratory (70%) systems.[11] Our case demonstrated some degree of involvement of the gastrointestinal, hematologic and mucocutaneous systems. Furthermore, the median duration of hospitalization reported by Feldstein et al. was 7 days, which is identical to our patient's duration of hospitalization, indicating a homogeneity in the duration of disease. However, our patient did not require mechanical

ventilation or placement in the ICU. Finally, immunomodulating therapies are being employed frequently in the management of this disease, with intravenous immune globulin (IVIG) (77%), glucocorticoids (49%), and interleukin-6 (IL-6) or Interleukin-1 inhibitors (20%) being most used.

Furthermore, it has been noted that a significant number of pediatric patients afflicted with MIS-C had underlying conditions (39%), including asthma (20%), neurologic (6%), diabetes (3%), obesity (2%), cardiac (3%), hematologic (3%) and oncologic (1%). Patients with underlying conditions

were also more likely to be hospitalized and to have a more severe course of disease.[12] However, our patient did not have any underlying conditions, which could possibly have resulted in the more indolent course of disease that was observed.

Our diagnosis of MIS-C in COVID-19 is further supported by reports of the observation of mesenteric adenitis in MIS-C who have undergone exploratory laparotomy, similar to our FACT findings of mesenteric adenitis.[10] Previously, the entry of SARS-CoV-2 into enterocytes has been demonstrated, indicating direct gastrointestinal infection.[13] In further support of this, viral shedding of SARS-CoV-2 in stool has previously been detected via stool RT-PCR.[14]

To conclude, we report a case of MIS-C in a COVID-19 positive child. MIS-C is a variable presentation of COVID-

19 and should be a differential in patients who fulfill the criteria but present with abdominal pain in the emergency. As the number of reports on this potentially fatal complication of COVID-19 increases, a coordinated effort to develop holistic guidelines for this condition must be undertaken by national and international governing bodies.

Consent to Publication: Author(s) declared taking informed written consent for the publication of clinical photographs/material (if any used), from the legal guardian of the patient with an understanding that every effort will be made to conceal the identity of the patient, however it cannot be guaranteed.

Authors Contribution: Author(s) declared to fulfill authorship criteria as devised by ICMJE and approved the final version. Authorship declaration form, submitted by the author(s), is available with the editorial office.

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