RESEARCH PAPER

Abdominal Manifestations of Multisystem Inflammatory Syndrome in Children: A Single-Center Experience

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Objectives: We reviewed the cases of probable multisystem inflammatory syndrome in children (MIS-C) to identify those cases that mimicked surgical emergencies. **Methods:** Records of children managed for MIS-C during a 15-month period between March, 2020 and April, 2021 were retrieved. Data on clinical presentation, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RT-PCR report, SARS-CoV-2 antibody status, blood investigations, radiological investigations and management were collected. **Results**: A total of 28 out of 83 children with probable MIS-C had acute abdominal symptoms and signs. Fifteen children had mild features like diffuse abdominal pain or non-bilious vomiting, and the remaining 13 (46.2%) had severe abdominal signs or bilious vomiting. Four children worsened with conservative treatment for MIS-C and were detected with perforated appendicitis. Two more children developed recurrent appendicitis on follow up. One child with appendicitis who underwent laparoscopic appendectomy, later manifested with MIS-C. **Conclusion:** Surgical abdominal emergencies may be confused with or occur concurrently in children with MIS-C that should be identified with a high index of suspicion.

Keywords: *Acute abdomen, Appendicitis, COVID-19, SARS-CoV-2, Surgery*.

Multisystem inflammatory syndrome in children (MIS-C) is a dreaded complication of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Abdominal pain can be a presenting feature of both coronavirus disease 2019 (COVID-19) and MIS-C. There exists a diagnostic dilemma in managing children with COVID-19 or MIS-C presenting with abdominal symptoms. This study aimed to identify management challenges of MIS-C mimicking surgical emergencies and delay in surgical management with probable MIS-C characteristics.

METHODS

This study retrieved records of children hospitalized with probable MIS-C from March, 2020 to April, 2021. Institutional review board (IRB) approval was obtained for the study.

MIS-C was diagnosed as per World health Organization (WHO) criteria [1]. The abdominal symptoms were graded mild for generalized abdominal pain and non-bilious vomiting, and severe for bilious vomiting, guarding and rigidity. All the children underwent tier 1 investigations like complete blood count (CBC), renal function test (RFT), liver function test (LFT), and C-reactive protein. Other tests like SARS-CoV-2 antigen, SARS-CoV-2 IgG and IgM antibody levels, serum ferritin, D-dimer levels, blood culture, echocardiogram and coagulation profile were done as tier 2 investigations. Ultrasonography (USG) of the abdomen was done when children had severe abdominal symptoms/ signs or when they had worsening of abdominal features. Data were collected on need for surgical manage-ment; and outcome and follow up data were collected in children with severe abdominal symptom/signs.

RESULTS

A total of 83 children were hospitalized as probable MIS-C. Twenty eight (33.7%) children had abdominal symptoms. Of these, 15 (53.6%) had mild symptoms and 13 (46.4%) had severe abdominal symptoms **Table I.**

Among 13 children with severe symptoms, dilated appendix and peri-appendicular inflammation was seen in nine children, and bowel wall edema in four children on sono-graphy. Six of these children were diagnosed with MIS-C and improved with conservative management; three of them required intravenous immunoglobulin, steroid and anticoagulant; and one child required steroid alone and two recovered with supportive care. Among those with severe symptoms, two children presented after 1-2 months with recurrent appendicitis and underwent laparoscopic appendectomy.

Table I Characteristics of Children With Abdominal Symptoms (*N*=28)

Features	*Mild abdominal symptoms (n=15)*	*Severe symptoms (n=13)*
Age, y[b]	9 (5-14)	10 (6-15)
Males	9 (60)	4 (30.8)
Interval till diagnosis, d[b]	7 (4-11)	6 (2-10)
Leucocyte count, $x10^9/L$[a]	2.4-17.4	12.2-26.8
CRP, mg/L[a]	50-480	12.4-282
D-dimer, ng/mL[a]	998 – >10,000	761-7331
Ferritin, mcg/L[a]	116-1967	227-846
SARS-CoV-2 positive[c]	15 (100)	9 (69.2)

Data presented as no. (%), [a]range or [b]median (range). [c]Either of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) antigen, IgG, or IgM positivity.

Four children with severe abdominal symptoms had a delay (range 2-8 days) in surgical management due to an underlying suspicion of MIS-C. In all four children, diagnosis was confirmed with radiological investigations like USG or CT abdomen. Surgical management was necessary for successful treatment; two had appendicular phlegm and two had acute perforated appendicitis that was managed with open appendectomy.

One other child who underwent appendectomy for suspected appendicitis had persistent fever spikes post-operatively. Investigations revealed high D-dimer, CRP and SARS-CoV-2 IgG positivity, and he was treated with single dose of intravenous immunoglobulin. A six-year-old male child presented with acute orchitis, which settled with conservative management. There were no deaths in these 28 children.

DISCUSSION

In this retrospective study, equal number of children with severe abdominal complaints were subsequently diagnosed as MIS-C or acute surgical abdomen. Children with severe abdominal complaints had a delay in surgical management with an initial suspicion of MIS-C. This was probably as these children were initially managed elsewhere as MIS-C and then transferred to our center.

The incidence of gastrointestinal manifestations like vomiting, abdominal pain and diarrhea in COVID-19 is reported between 6-13% [2]. There are reported cases of pseudo-appendicitis, appendicitis or complicated appendicitis with COVID-19 [3-6]. The postulated cause for this association was SARS-CoV-2 binding with ACE-2 receptors in the gastrointestinal tract, resulting in hyper-inflammation, dysregulation of immune cells, and a prothrombotic state with organ ischemia [5].

Acute abdomen has been reported in one-third children with MIS-C, postulated to be due to underlying severe intestinal vasculitis [7]. Children with suspected acute appendicitis were noted to develop postoperative fever and shock following appendectomy [8,9]. They required immunomodulators, steroids and rarely, repeat surgical exploration [10]. Histopathological examination of the resected specimens showed transmural chronic inflammation, extensive venous microthrombi, and markedly inflamed mesentery, that favored MIS-C as an etiology.

A systematic review of acute abdomen in MIS-C reported that abdominal surgery was unnecessary in half of the children with MIS-C [11]. Conversely, one-fourth of children with MIS-C had a surgical pathology. The imaging findings were discriminatory for surgical abdomen in MIS-C unlike laboratory markers, similar to the present study.

Appendicitis or terminal ileal thickening is common during the inflammatory phase of COVID- 19 infection or in children with MIS-C. Most of them improve with conservative management. Instead, operative management may lead to stormy postoperative period and high morbidity [9,10]. As a corollary of intestinal ischemia (hypothesized as a complication due to intestinal vasculitis), we may consider ruling out cardiac involvement in MIS-C by an echocardiogram, before operating upon children with surgical complications [12].

A multinational experience from Latin America [13] reported age more than 5 years to be associated with a higher risk of appendicitis. However, contrary to our study, they did not note a delay in diagnosis of acute appendicitis in their patients [13].

Testicular torsions have been reported during COVID-19 pandemic [14], similar to a single case of acute orchitis in the present study. This could result from higher expression of ACE2 receptors in the testes and can be related to inflammatory and vasculitis changes occurring during COVID-19 or MIS-C. Acute pancreatitis has also been reported as one of the causes of abdominal pain in children with MIS-C [15]. There was no child with acute pancreatitis in this study group.

To conclude, MIS-C and surgical abdomen are close mimickers. Severe illness, shock out of proportion to the clinical findings, presence of high-grade fever, contact history with COVID-19 positive patient, and COVID IgG positivity can help in differentiation of these two. A multidisciplinary team with physician, surgeon, radiologist and intensivist can help in managing these children timely and effectively.

WHAT THIS STUDY ADDS?

- Severe abdominal signs may occur in a significant proportion of patients with multisystem inflammatory syndrome in children (MIS-C).
- Surgical abdominal emergencies may mimic MIS-C and should be identified timely.

Ethics clearance: Ethical clearance obtained from institutional review board
Contributors: AKU-manuscript writing and data analysis; RP-data collection; LS-review of the manuscript and corrections; JS-manuscript review and corrections. All authors aproved the final version of the manuscript.
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