The rising appendicitis mimicker: A case report of Multisystem Inflammatory Syndrome in Children presenting with acute abdomen

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Abstract
We describe a case of post-coronavirus disease 2019 (COVID-19) multisystem inflammatory syndrome in children (MIS-C). The 12-year-old child presented with appendicitis-like symptoms in the form of gradually worsening abdominal pain localizing over the right iliac fossa, fever, and vomiting. After an appendectomy, the abdominal pain did not resolve. He later developed orthopnea, bilateral lower limb pitting edema, and bilateral fine basal crepitations. This pointed to MIS-C. We should be mindful of multisystem inflammatory syndrome in children with a recent history of COVID-19.

Keywords
Pediatric inflammatory multisystem syndrome, COVID-19, fever, pediatrics, abdominal pain

Introduction
Multisystem inflammatory syndrome in children (MIS-C) may occur weeks after coronavirus disease 2019 (COVID-19) and is described as a hyperinflammatory response affecting multiple systems. It can even occur after an asymptomatic severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. A study analyzing reported cases of MIS-C in patients younger than 21 years old found that 80% of patients had gastrointestinal symptoms on presentation. This was the most prevalent symptom in patients 6–20 years old. A recent meta-analysis found that gastrointestinal involvement was present in 84.3% of MIS-C cases. In New York State, between 1 March and 10 May 2020, the incidence of MIS-C in those younger than 21 years was 2 per 100,000. We describe an MIS-C patient whose initial presentation resembled appendicitis.

Case report
A previously healthy 12-year-old Middle Eastern male presented to the emergency room with gradual progressive right lower abdominal pain of 1-day duration and fever of 40°C. Three days before admission he was complaining of vomiting and persistent fever of 38°C for which a pharmacist has prescribed antipyretics and antibiotics. He was diagnosed with appendicitis and underwent open appendectomy without prior imaging or laboratory investigations. The appendix looked normal macroscopically. Two days after the surgery, the COVID-19 reverse transcriptase polymerase chain reaction (RT-PCR) assay was negative. Five days later, surgical wound and blood samples were taken for culture as the fever was unremitting and the patient had developed conjunctivitis. He was started on broad-spectrum antibiotics. The surgical wound culture was positive for pseudomonas and the blood culture was negative. Ten days post appendectomy there was diffuse abdominal pain. Abdominopelvic computed tomography (CT) scan with contrast revealed few enlarged reactionary mesenteric lymph nodes, minimal free fluid in the right iliac fossa, and hepatomegaly of 15 cm in the largest diameter (Figure 1). A rapid
test for SARS-CoV-2 was performed which returned positive for IgG anti-SARS-CoV-2 antibodies and negative for IgM anti-SARS-CoV-2 antibodies. The fever persisted for 2 weeks post-appendectomy. He also developed orthopnea, bilateral lower limb pitting edema, and bilateral fine basal crepitations. Electrocardiogram (ECG) showed normal sinus rhythm. Cardiac troponin I was elevated with normal creatinine kinase (CK)-total and CK-MB, and echocardiogram showed average caliber coronary arteries, average left ventricular dimensions with an ejection fraction of 76%, mild tricuspid regurgitation with right ventricular systolic pressure of 30 mm Hg, mild mitral regurgitation, congested inferior vena cava, and no pericardial effusion (Table 1). He was diagnosed with myocarditis and was administered diuretics. He did not require pharmacologic or mechanical circulatory support. Four days later, a repeat echocardiogram was normal showing only trivial mitral regurgitation and tricuspid regurgitation. Chest CT without contrast revealed bilateral mild pleural effusion. The CT image was assessed as COVID-19 Reporting and Data System (CO-RADS) category 1. CO-RADS is a standardized assessment tool for pulmonary involvement in COVID-19 patients. On a 0 to 6 scale, 1 implies a very low level of suspicion for pulmonary involvement.5

The patient was transferred to the pediatric intensive care unit (PICU) for close follow-up of myocarditis where he started 1 g/kg/day intravenous immunoglobulin (IVIG) over 2 days, a prophylactic dose of low-molecular-weight heparin (LMWH), and 30 mg/kg pulse corticosteroids for 3 days. This was followed by corticosteroids at 2 mg/kg for 1 month, after which they will be gradually withdrawn. The LMWH was administered as prophylaxis until hospital discharge due to the patient’s elevated d-dimer levels. Following that, he will be switched to aspirin for 6 months.

In total, the patient was admitted for 25 days, of which six were in the PICU. The patient was discharged after the inflammatory markers had decreased and will follow-up with echocardiography for 6 months.

**Discussion**

Persistent fever, abdominal pain, vomiting, and myocarditis in this child along with laboratory evidence of inflammation, negative blood cultures, prolonged hospitalization, and positive COVID-19 serology meet the criteria for MIS-C according to the Centers for Disease Control and Prevention (CDC). Laboratory evidence of inflammation included elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), d-dimer, and ferritin. Laboratory investigations also revealed neutrophilia, hypoalbuminemia, and thrombocytosis. The thrombocytosis in this case could have been a side effect of corticosteroids therapy. The persistence of diffuse abdominal pain post-surgery was attributed to the mesenteric adenitis found on CT as investigations for other causes of the abdominal pain turned out negative. Mesenteric adenitis is one of the differential diagnoses of appendicitis because of the similar abdominal pain pattern. Since mesenteric adenitis was also noted in other MIS-C cases, we are suggesting that there might be an association between mesenteric adenitis and the abdominal pain manifestation of MIS-C.

Gastrointestinal symptoms commonly occurring in MIS-C can be the presenting symptom in most children and can be misdiagnosed as appendicitis or viral gastroenteritis. The presence of fever, rash, and conjunctival hyperemia should raise concern for MIS-C as such patients can deteriorate due to other system affection. In an observational study in 81 children presenting with acute abdominal pain, those with MIS-C were more likely to experience severe vomiting, longer duration of abdominal pain and fever, and higher grades of fever compared to children with appendicitis. Lab findings showed a higher neutrophil count, higher inflammatory markers, and lower lymphocytic count in the MIS-C group. On abdominal ultrasonography, children with MIS-C were more likely to have ascites, terminal ileitis, and mesenteric adenitis than children with appendicitis. It is worth noting that appendicitis can be concomitantly present in patients with MIS-C and these patients may present with severe symptoms up to shock out of proportion to their findings of appendicitis.

This case report adds to the literature of the newly discovered MIS-C. It serves as an example of asymptomatic SARS-CoV-2 complications in children. Since the excised appendix was not studied histopathologically, the report cannot ascertain that it was a misdiagnosis. However, emergency doctors, pediatricians, and pediatric surgeons should be mindful of
the overlap of MIS-C and appendicitis presentations while further studies are performed to better differentiate the two.

**Conclusion**

Due to the insufficient understanding of MIS-C, the appendicitis-like presentation led the unsuspecting surgical team to proceed with an appendectomy without deeper investigations. This led to a delay in diagnosis of MIS-C, surgical complications, and prolongation of hospital stay. Since MIS-C may present primarily with acute abdomen, like appendicitis, we expect that early diagnosis and high suspicion of MIS-C will lower the incidence of unnecessary appendectomies. Specifically, we recommend that further studies investigate the addition of ultrasound in the assessment of children with suspected appendicitis if they have a recent history of COVID-19 or exposure to COVID-19. We speculate that adding MIS-C into consideration in the suspected appendicitis guidelines might lead to fewer unnecessary appendectomies.

**Acknowledgements**

We thank Dr Marwa Mohamed (Ain Shams University) for providing a second opinion on the computed tomography studies.

**Declaration of conflicting interests**

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

**Funding**

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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### Table 1. Summary of relevant lab values.

| Laboratory         | Day 9 | Day 11 | Day 12 | Day 14 | Day 15 | Day 16 | Day 17 | Day 18 | Day 19 | Day 22 |
|--------------------|-------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| CRP (0–6, mg/L)    | 370.4 |        |        | 212.3  |        | 44.9   |        | 8.2    |        |        |
| ESR (First hour: 2–20, mm/h) |        | 85     |        | 110    | 100    | 60     |        |        |        |        |
| Ferritin (6–320, ng/mL) | 562    |        |        | 497.1  |        | 344.1  |        |        |        |        |
| LDH (140–271, IU/L) | 275    | 339    | 370    |        | 234    |        |        |        |        |        |
| d-Dimer (0–0.55, µg/mlFEU) | 2.06   | 4.42   |        |        |        |        |        |        |        |        |
| Troponin-I (0–0.03, ng/mL) | 0.417  | 0.355  |        |        |        |        |        |        |        |        |
| WBC (4–10, 10³/µL) | 9.6    | 14.4   | 11.3   | 9.5    | 11.9   | 11.7   |        |        |        |        |
| Neutrophils (2–7, 10³/µL) | 8.3    | 12.4   | 8.4    | 7.47   | 8.52   | 8.4    |        |        |        |        |
| Lymphocytes (1–3, 10³/µL) | 1.20   | 1.48   | 1.90   | 1.91   | 1.51   | 2.41   | 2.46   |        |        |        |
| HGB (13–17, g/dL) | 9.9    | 9.4    | 8.9    | 10.2   | 10.3   | 10.7   |        |        |        |        |
| Platelets (150–450, 10³/µL) | 164   | 239    | 410    | 691    | 713    | 565    |        |        |        |        |
| Amylase (28–100, U/L) |        |        |        |        |        |        |        |        |        |        |
| Lipase (0–160, U/L) |        |        |        |        |        |        |        |        |        |        |
| Sodium (138–145, mmol/L) | 140   | 141    | 139    | 142    | 137    | 133    |        |        |        |        |
| Albumin (3.5–5.2 g/dL) | 2.8    | 3.5    | 3.1    | 3.4    |        |        |        |        |        |        |
| AST (13–39, IU/L) | 17     | 17     | 27     | 26     | 23     |        |        |        |        |        |
| ALT (7–52, IU/L) | 11     | 12     | 13     | 14     | 13     |        |        |        |        |        |

Normal range is included in parenthesis for reference. Days are in reference to admission. Extreme values are highlighted in bold. AST: aspartate aminotransferase; ALT: alanine aminotransferase; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; HGB: hemoglobin; LDH: lactate dehydrogenase; WBC: white blood cells.
Ethical approval

Ethical approval is not required for a case report without patient identifying information.

Informed consent

Written informed consent for publication was obtained from the legally authorized representative of the minor subject.

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