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Pediatric appendicitis in times of COVID-19: Think MIS-C

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ABSTRACT

We report two cases of children presenting with clinical and radiological findings suggestive of acute appendicitis. Both patients underwent appendectomy and were subsequently diagnosed with multisystem inflammatory syndrome in children (MIS-C). Histopathology revealed reactive lymphoid follicle hyperplasia in one patient and acute appendicitis in the other. Both patients required admission to the pediatric intensive care unit after surgery and were treated successfully with immunotherapy for MIS-C.

1. Case report

1.1. Case 1

A 7-year-old previously healthy girl presented to the emergency department (ED) with a 4-day history of fever and abdominal pain that were initially associated with vomiting and diarrhea. On physical examination, she had a temperature of 38.4 °C, tachypnea, tachycardia, and maintained hemodynamics after intravenous fluid administration. A non-purulent conjunctivitis was noted bilaterally, and mild abdominal distention with right iliac fossa tenderness was elicited upon palpation. The initial complete blood count (CBC) revealed leukopenia (4.0 × 10⁹/L), with lymphopenia (0.7 × 10⁹/L), and thrombocytopenia (66,000/mm³). Inflammatory markers were elevated, including C-reactive protein (CRP) (66 mg/L), procalcitonin (3.95 ng/ml), and ferritin (1939 ng/ml). Abdominal ultrasonography showed a mildly enlarged appendix measuring (0.7 cm) on maximum diameter surrounded by a moderate amount of free fluid without appendicolith or wall defects. Her computed tomography (CT) scan endorsed similar findings of an intact, fluid filled, and enlarged appendix measuring (0.6 cm) with clear wall enhancement. Given the clinical and radiological findings that support acute appendicitis, the decision was made for laparoscopic appendectomy. Surprisingly, a non-inflamed appendix was observed intraoperatively. The patient developed hypotension and desaturation afterward that required pediatric intensive care unit (PICU) admission for inotropic support and oxygen supplementation. Further history clarified that the girl had been in contact with a confirmed coronavirus disease 2019 (COVID-19) case two weeks prior to her presentation. Her severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) polymerase chain reaction (PCR) testing came back positive. N-terminal pro-B-type natriuretic peptide (NT-pro BNP) was elevated (2997 pg/mL) as was D-dimer (3.74 μg/ml). Echocardiography reflected normal coronary arteries with normal cardiac function. Immunotherapy for MIS-C with intravenous immunoglobulin (IVIG) and IV methylprednisolone was initiated with remarkable clinical improvement. Broad-spectrum antibiotics were administered empirically till her cultures came back negative.

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Later, the histopathology of appendiceal tissue was reported as reactive lymphoid follicular hyperplasia. The girl was eventually discharged from the hospital in stable clinical condition after being given an oral prednisolone tapering regimen and low-dose aspirin.

1.2. Case 2

A previously healthy 10-year-old girl presented to the ED with a 2-day history of fever, headache, abdominal pain, vomiting, and diarrhea. Two weeks earlier, she had been experiencing anosmia at the same time she tested positive for SARS-CoV-2 PCR. In the ED she was febrile (38.1 °C), her abdomen was mildly distended with rebound tenderness in the right iliac fossa, and she had positive Rovsing’s sign. Laboratory results revealed leukocytosis (16 × 109/L), normal platelet count (302/mm3), elevated acute phase reactants (CRP) (41 mg/L), erythrocyte sedimentation rate (ESR) (46 mm/hr), and ferritin (1408 ng/ml). Abdominal ultrasonography demonstrated a non-compressible tubular structure with one blind end in the right iliac fossa measuring (1.6 × 1.5 cm) along with an appendicolith and inflammation that was suggestive of acute appendicitis. The girl was taken for appendectomy and intraoperatively her appendix was obviously inflamed but intact. Her clinical status was deteriorating further and she remained intubated post-operatively. Bilateral diffuse ground-glass opacities were seen in her chest radiograph. Normal cardiac function and prominent coronary arteries without aneurysms were detected on echocardiography. The levels of NT-pro BNP (1044 pg/mL), and D-dimer (5.598 μg/mL) were both increased. The additional findings, together with the patient’s medical history, led to the diagnosis of MIS-C, which prompted the consideration of anti-inflammatory and prophylactic anticoagulant therapies. The patient’s condition significantly improved after IVIG and IV methylprednisolone. Prophylactic enoxaparin was stopped due to the development of a brief pulmonary hemorrhage. Her hospital stay was complicated by a Candida glabrata blood stream infection that was treated successfully with liposomal amphotericin B. Empirical antibiotics were given for a short period until bacterial infection had been ruled out. The histopathology report was consistent with acute appendicitis, and the appendiceal lumen was filled with fecal material. Ultimately, the patient went home in good health.

2. Discussion

Multisystem inflammatory syndrome in children (MIS-C) is a post-infectious condition related to immune dysregulation occurring weeks after acute SARS-CoV-2 infection. The Centers for Disease Control and Prevention (CDC) issued a case definition for MIS-C including a severe illness requiring hospitalization in individuals <21 years of age and presenting with fever for ≥24 hours, laboratory evidence of inflammation, multisystem (≥2) organ involvement, and a recent SARS-CoV-2 infection or exposure within four weeks prior to the onset of symptoms. Organ systems commonly involved in MIS-C include gastrointestinal (92%) and cardiac (80%) [1]. Gastrointestinal symptoms of MIS-C include abdominal pain, vomiting, diarrhea, and manifestations that can mimic acute appendicitis (AA) including mesenteric adenitis and terminal ileitis [2]. Surgically confirmed cases of AA have been described in patients with MIS-C [3,4]. Due to the predominance of gastrointestinal manifestations and possibly absence of systemic features in some patients with MIS-C during the initial presentation, it can be challenging to recognize MIS-C in patients with concomitant AA. In a case series in Cape Town, three children with confirmed AA were diagnosed with MIS-C after appendectomies and all required admission to a high or intensive care unit [3]. Early recognition of MIS-C in patients with a clinical presentation mimicking surgical abdomen is prudent to avoid unnecessary surgery considering the increased risk of perioperative morbidity in these patients [5]. Non-operative treatment of uncomplicated AA with antibiotics in children with COVID-19 has been reported [6,7]. Patients with AA and MIS-C are likely to undergo operative management due to the severe presentation of MIS-C that may lead to the clinical decision of surgical intervention. Anderson et al. reported successful management of a patient with AA in whom concomitant MIS-C was recognized and treated with IVIG, antibiotics, and inotropic support until the patient’s condition was deemed stable for surgery. Operative treatment was decided due to the presence of a fecalith, and a perforated appendicitis was identified. Post appendectomy, interleukin (IL)-1 receptor antagonist (anakinra) was administered instead of corticosteroids due to concerns of an infectious process [4]. In conclusion, our report highlights that MIS-C can mimic AA and that both conditions can simultaneously occur to increase the awareness of pediatric surgeons to this syndrome. Utilizing a multidisciplinary medical and surgical team approach and obtaining relevant laboratory investigations and imaging studies can facilitate early recognition and treatment of MIS-C and plan the appropriate timing of surgical intervention for AA in MIS-C.

3. Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

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Authorship

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Declaration of competing interest

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