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Case Series

Variability of COVID-19 and MIS-C Related Abdominal Surgical Presentations in Children: Case Report Series

Engelis A[1,2], Zviedre A[1,2], Pavare J[3,4], Zurmutai T[1,2], Berezovska MM[1,2*], Bormotovs J[5], Laizans P[1,6], Petersons A[1,2]

[1]Department of Pediatric Surgery, Children's Clinical University Hospital, Vienibas gatve 45, Riga, Latvia, LV-1004
[2]Department of Pediatric Surgery, Riga's Stradins University, Dzirciema iela 16, Riga, Latvia, LV-1007
[3]Department of General Pediatrics, Children's Clinical University Hospital, Vienibas gatve 45, Riga, Latvia, LV-1004
[4]Faculty of Medicine at Riga's Stradins University, Dzirciema iela 16, Riga, Latvia, LV-1007
[5]Department of Anesthesiology and Intensive Care, Children's Clinical University Hospital, Vienibas gatve 45, Riga, Latvia, LV-1004
[6]Department of Pediatric Surgery, University of Latvia, Raina Bulvaris 19, Riga, Latvia, LV-1586

[*]Corresponding Author: Marisa Maija Berezovska, Department of Pediatric Surgery, Children's Clinical University Hospital, Vienibas gatve 45, Riga, Latvia

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1. Introduction

The WHO declared Coronavirus Disease 2019 (COVID-19), a pandemic on the 11th of March in 2020 [1]. In April 2020, cases of hyperinflammatory shock in children associated with previous COVID-19 infection emerged, now this condition is known as multisystem inflammatory syndrome in children (MIS-C). Patients with MIS-C usually present with persistent fever, skin rash, mucocutaneous lesions, gastrointestinal symptoms, and in severe cases, hypotension, myocarditis and shock. Majority of MIS-C patients present to the emergency department with fever and gastrointestinal symptoms, like severe abdominal pain, diarrhea, emesis and anorexia, which may mimic acute surgical pathologies, thus bringing potential pitfalls in decision making for pediatric surgeons [2-5].

Reports of MIS-C mimicking acute abdominal pathology leading to surgery are increasing. Gerall et al. emphasize the necessity of recognition of MIS-C in heavily COVID-19 affected areas as to evade unnecessary surgery for previously exposed patients. Although diagnostic and therapeutic guidelines are already published, they are constantly updated as new information and data are developed. Intravenous immunoglobulins and corticosteroids are widely used for treatment of MIS-C. Anakinra and vasopressors are recommended in severe cases [6].

Jackson et al. report a case of terminal ileum inflammation in MIS-C, which mimicked acute appendicitis in a preoperative ultrasound and was treated with appendectomy and resection of the terminal ileum segment. Histology showed vasculitis of mesenteric vessels, hyperplastic Peyer's patches, necrotizing mesenteric lymphadenitis, bowel and appendiceal wall edema [7]. In a case series, Sahn et al. present a patient with MIS-C, who developed bowel obstruction symptoms and despite treatment with intravenous immunoglobulins, undergone ileocolic resection. Histology showed similar findings - transmural ileum lymphatic inflammation, vasculitis, and necrotizing lymphadenitis. Electron microscopy of ileum showed no viral particles [8]. Both cases show features of systemic hyperinflammation rather than those of inflammatory bowel disease or acute appendicitis.

Latvia experienced a very mild first wave of the COVID-19 pandemic, with the first surge in newly diagnosed COVID-19 cases beginning in October 2020 and peaking in January 2021. The first local MIS-C case was registered in January 2021. As new COVID-19 cases dwindle, the Children's Clinical University Hospital (CCUH) in Riga is treating an increasing number of MIS-C patients [9].

2. Case Presentation

Three patients' medical records were analyzed as their parents provided consent to participate in this non-interventional study, therefore, approval by an ethics committee was not required. The first case presents a 16-year-old girl with an acute COVID-19 infection, while the other two cases demonstrate a four-year-old girl and a 17-year-old boy with MIS-C, who underwent emergency surgical interventions. The patient cases are analyzed in Table 1 for side-by-side comparison through clinical symptoms, laboratory and radiological diagnostics, and medical and surgical management.

Criteria	**Case No 1**	**Case No 2**	**Case No 3**
Age (years)	16	4	17

Sex		F	F	M
Diagnosis (incl. MIS-C)		Covid-19 infection Ovarian apoplexy Chronic appendicitis	MIS-C	MIS-C Mesenteric lymphadenitis
Clinical symptoms	Fever	Yes	Yes	Yes
	Severe illness	No	Yes	Yes
	Two or more organ systems involved	No	Yes	Yes
	Days of symptoms before surgery	2	4	2
	Abdominal pain	Yes	Yes	Yes
	Emesis	Yes	Yes	No
	Diarrhea	No	Yes	No
Inflammation	CRP, mg/l	0.4	↑ 237	↑ 358,35
	ESR, mm/h	Not performed	↑ 55	↑ 46
	Fibrinogen, g/l	Not performed	3.91	↑ 7,16
	D dimer, mg/l	Not performed	↑ 3,44	↑ 8,99
	Ferritin, ng/ml	Not performed	242.7	↑ 881,9
	LDH, U/l	Not performed	↑ 316	↑ 337
	IL-6, pg/ml	6.28	↑ 173	↑ 575
	Neutrophil, $\times 10^3$/mkl	5.65	↑ 14,21	↑14,06
	Lymphocyte, $\times 10^3$/mkl	3.26	↓ 1,4	↓ 0,45
	Serum albumin, g/l	Not performed	↓ 20,8	↓ 28,17
	Blood culture	Negative	Negative	Negative
Other laboratory findings	Creatinine, µmol/l	Not performed	↓ 21,82	76.79
	Urea, mmol/l	Not performed	↓ 2,15	3.24
	troponin I, ng/l	Not performed	↑ 148,8	Not performed
	NT pro-BNP, pg/ml	Not performed	↑ 20199	Not performed
SARS-CoV-2	PCR	Positive	Negative	Negative
	Serology	Not performed	IgG positive, IgM negative	Positive
	Antigen test	Not performed	Negative	Negative

	prior four-week exposure	Yes	Yes	No
Exclusion - no alternative diagnosis		N/A	Yes	Yes
Surgery	Access	Diagnostic laparoscopy	Diagnostic laparoscopy	Diagnostic laparoscopy
	Intraoperative finding	Apoplexy of right ovary Chronic appendicitis Sanguineous fluid	Distended intestinal loops Appendix intact. Yellow, cloudy, viscous fluid	Enlarged hemorrhagic mesenteric lymph nodes. Greenish, cloudy fluid
	Histology	Appendix with lymphocyte infiltration, full-blooded.	Enlarged lymph nodes not detected	Not performed
Imaging	Abdominal US	Not performed	Acute mesenteric lymphadenitis	Mesenteric lymphadenitis
	Pleural US	Not performed	Not performed	Bilateral pleural effusion
	Abdominal X-ray	Not performed	Paralytic ileus	Ileus with air-fluid levels
	Thorax X-ray	Not performed	Left side basal pneumonia, bilateral minimal pleural effusion	Without pathology
	Abdominal CT	Not performed	Not performed	Mesenteric lymphadenitis, free intra-abdominal liquid, thickened walls in terminal ileum
	Thorax CT	Not performed	Bilateral polysegmental pneumonia without gangrene with minimal pleural effusion	Bilateral viral inflammation, left side basal fibrosis, bilateral pleural effusions
	Echocardiogram	Not performed	Minimal mitral and tricuspid valve regurgitation, increased pericardial effusion	Slight mitral valve regurgitation, decreased left ventricular systolic function
Management	PICU admission	No	Yes	Yes

	Steroids	No	Yes	Yes
	Antibiotics	Yes	Yes	Yes
	Aspirin	No	Yes	Yes
	Respiratory support	No	Yes	Yes
	Hospital stay duration, d	4	17	18
F, female; M, male; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; LDH - Lactate dehydrogenase; Il-6, Interleukin 6; PCR, polymerase chain reaction; PICU, pediatric intensive care unit; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; d, day; US, ultrasound; CT, computed tomography.				

Table 1: Clinical characteristics and case definitions of children.

3. Discussion

According to the currently available literature, COVID-19 infection may be associated with acute appendicitis in children [10]. There are two main reasons for this: SARS-CoV-2 causes persistent gastrointestinal (GI) infection (detectable viral RNA in fecal samples) and could induce lymphoid follicular hyperplasia of the colonic epithelium lining the appendix leading to lumen inflammation and obstruction [11, 12].

In Case No 1, considering the patient's clinical and laboratory picture, as well as the medical history, there is no reason to contemplate that acute appendicitis is associated with COVID-19 infection. The case was a rather mild COVID-19 in adolescent with fever, but without inflammatory signs such as leukocytosis, lymphopenia, high levels of C-reactive protein and interleukin-6. There was a history of chronic appendicitis and an acute gynecological pathology - right ovarian apoplexy, which was detected only during laparoscopy; however, the ambiguous symptoms lead to the surgical judgment. Acute complicated appendicitis is determined at a higher rate during emergency surgery in patients with COVID-19 infection [10]. In this regard, our case is different: the pathologic examination of the appendix showed lymphocyte infiltration, lipomatosis, and fibrosis, i.e. chronic inflammation signs without any specific changes, which could be linked to COVID-19 infection. MIS-C is an uncommon complication of COVID-19 that has a clinical presentation similar to Kawasaki disease, bacterial sepsis, toxic shock syndrome, and acute complicated appendicitis [13, 14]. The age of the patients with MIS-C is observed ranging from six months to 20 years, the median ages from the reported studies are between 3.5-16 years [15].

As presented above, our two patients with MIS-C were at age of four and 17 presenting with fever, severe abdominal pain and vomiting. This resembled the presentation of acute complicated appendicitis. Per the local algorithm of acute appendicitis at the CCUH, these two cases were indicated for surgical treatment [16]. Diagnostic laparoscopy was performed for both patients and yellow purulent peritoneal fluid was detected in both cases and additionally,

hemorrhagic mesenteric lymphadenitis in Case No 3. There was no visual evidence of the inflammatory changes in appendiceal wall for both patients. The same observation can be found in other publications, such as a nine-year-old girl, who presented with fever and GI symptoms for two days. She had a suspicion for acute appendicitis, underwent conventional appendectomy, however, the pathologic examination of the resected appendix revealed findings that were discordant with the diagnosis of acute appendicitis [7].

Appendectomy was not performed in our two patients with MIS-C, while they had a positive screen for COVID-19 antibodies and the findings were most consistent with MIS-C. There is a report about a 12-year-old boy who visited the emergency department with complaints of fever and abdominal pain, therefore, acute appendicitis could not be ruled out. Before the admission to the hospital, an abdominal CT scan was performed, which exposed enlarged lymph nodes with suspicious internal necrosis in the right lower quadrant (RLQ) of the mesentery without demonstrable abnormal bowel wall thickening, including the appendix [17].

According to the initial radiological diagnostic results (US and CT) in the emergency department, there were enlarged lymph nodes in RLQ without thickening of appendix for Case No 3. Hemorrhagic lymphadenitis was found during laparoscopy, but the histological sample was not obtained because a MIS-C diagnosis was not yet established, and a simpler origin of primary peritonitis was suspected. Considering these diagnostic results, radiologists have an important role to initially evaluate the imaging findings of MIS-C associated with COVID-19 in children. Improved radiological recognition may allow the patient to escape the emergency surgical intervention and unnecessary appendectomy.

There is a retrospective study that includes 16 patients with fever and some with GI symptoms between April and May 2020. Abdominal imaging findings were as follow: small-volume ascites, hepatomegaly, increased renal echogenicity, bowel wall thickening, gallbladder wall thickening, mesenteric lymphadenopathy, splenomegaly, and urinary bladder wall thickening [18]. Although the abdominal imaging features of MIS-C are nonspecific, they should alert the radiologist to the possible diagnosis of MIS-C associated with COVID-19 in children [19].

Nevertheless, our two MIS-C cases that had clinically suspicion for acute complicated appendicitis, the decision to perform diagnostic laparoscopy was not considered a mistake. In Latvia, there is only the inception of MIS-C cases during COVID-19 pandemic. In the near future, the differential diagnosis for acute complicated intraabdominal surgical infection will also include MIS-C and pediatric surgeons need to consider it. In contrast to acute Covid-19 infection in children, MIS-C appears to be a condition of higher severity with 68% of cases having required critical care support [5].

Our experience demonstrates that we need to be ready for patients, whose MIS-C, developing after asymptomatic COVID-19 infection, may present with serious acute abdominal symptoms requiring surgical intervention. Concurrently, we presumably will not find any major surgical complications on diagnostic laparoscopy. Given the current COVID-19 pandemic, when patients present acute abdominal pain with fever, hemodynamic instability and high markers of inflammation, closer attention of the epidemiological history of COVID-19 and MIS-C syndrome needs to be highlighted. In case of MIS-C suspicion, screening tests are recommended, however, a multidisciplinary approach should be utilized.

Conflict of Interest

All authors declare no conflicts of interest.

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