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Abdominal manifestation of multisystemic inflammatory syndrome in children

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ABSTRACT

Summary: Multisystemic inflammatory syndrome (MIS-C) can develop as a complication of SARS CoV-2 infection, involving the gastrointestinal system mainly by vasoconstriction, edema, glandular hyperplasia, and a procoagulant state leading to direct tissue injury.

Method: ology: a series of cases including 8 patients with MIS-C treated in two highly complex institutions is presented. These patients, had abdominal symptoms of surgical management.

Results: The average age was 9.5 years and the most frequent symptoms were fever, abdominal pain, diarrhea (100%); in addition, 87.5% presented shock. The diagnosis of SARS CoV-2 was confirmed by RT-PCR test in 37.5%, antigen 12.5% and the rest of the patients showed IgM and IgG antibodies. In laboratories, the increase in acute phase reactants, Erythrocyte Sedimentation Rate (ESR), C-reactive protein, procalcitonin, as well as troponin, D dimer and proBNP, is highlighted. The surgical outcome documented 2 patients with a normal appendix, 3 patients with edematous appendicitis, and 3 patients with complicated appendicitis.

Conclusions: patients with MIS-C display abdominal symptoms similar to those present in surgical emergencies and a non-negligible number of cases require surgical exploration. This condition poses a new differential diagnosis to the surgical abdomen in pediatric patients.

1. Introduction

The SARS CoV-2 pandemic, declared by the World Health Organization (WHO) on March 11, 2020, since the beginning has had a differential behavior between children and adults, mainly due to the type of involvement, clinical manifestations and severity. Thus, in

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mid-May 2020, European researchers reported cases of patients with symptoms of severe inflammation and multisystemic involvement that was initially associated with a syndrome similar to Kawasaki disease [1–4]. From this description and the issue of the criteria both by the WHO and the Center for Disease Control and Prevention (CDC) a new differential diagnosis has been established in children with gastrointestinal symptoms and surgical abdomen [1,3,5–8].

The multisystemic inflammatory syndrome, developed by patients as a complication of SARS CoV-2 infection, is a rare entity but one that can involve important organs of the body's economy in a variety of ways [2,9–12]. The clinical manifestations at abdominal level can lead to suspicion of surgical abdomen pathology, mainly acute appendicitis, without documentation of macroscopic or pathological findings in some cases that explain this entity [2,3,9,13].

Gastrointestinal involvement in patients with SARS CoV-2 infection is related to the presence of angiotensin converting enzyme receptors in the intestinal and vascular epithelium, especially in glandular cells, absorptive enterocytes of the distal ileum and colon, which ultimately favor vasoconstriction, edema, glandular hyperplasia and a procoagulant state that leads to direct tissue damage is encouraged [5,8,12,14,15].

2. Presentation of the cases

The city of Neiva as a reference place in the South Colombian region, admit pediatric patients with medium and high complexity medical and surgical pathologies from regions of Huila, South of Tolima, Eastern Cauca, Caquetá, Putumayo, Amazonas and even from some other regions of the Country (Colombia). The information was collected in 1-year period, after the scientific report issued by the WHO about the multisystemic inflammatory syndrome associated with SARS CoV-2, in two institutions of IV-level complexity. The information was obtained from the records of the medical histories from May 15, 2020 to May 14, 2021. Patients who met the diagnostic criteria of MIS-C were included in accordance with the criteria issued by the WHO's scientific committee (Table A1).

3. Results

During the study year, 34 patients met the MIS-C diagnostic criteria and 8 of them required abdominal surgical management. In Table A2 the data of these patients are showed. From this 8-patient group, 62.5% were female. The average age was 9.5 years. Regarding the clinical manifestations, it was documented that 100% of the patients had fever, abdominal pain and diarrhea. Vomiting was observed in 87.5%, followed by rash (62.5%) and the least frequent finding was conjunctivitis (25%). Due to the fact that 87.5% of the patients presented shock, it was advised to be managed at the pediatric intensive care unit. None of the patients had a significant medical history. Overweight and obesity occurred in 25%, the rest of the patients showed appropriate nutritional condition.

The diagnosis related to SARS CoV-2 infection was documented by RT PCR, antigen or serological tests (IgG or IgM), 37.5% presented active infection with RT PCR or positive antigen, the rest of the patients had a diagnosis of past infection.

The surgical finding reported 2 patients with normal appendix, 3 patients with edematous appendicitis and 3 patients with complicated appendicitis. Cardiovascular involvement is documented by the presence of shock (87.5%), need for vasoactive support (75%), and coronary abnormality (62.5%).

The current treatment was optimized following the clinical recommendations available each time of patient care, immunoglobulin (100%), steroid (25%) and Acetylsalicylic Acid (ASA) (87.5%) were administered.

The hematological analysis documents leukocytosis (median 16,315), elevated ESR (median 31 seconds), elevated C-reactive protein (median 26mg/dl), elevated procalcitonin (median 5.1), as well as elevated values of cardiovascular involvement on admission troponin, D-dimer and elevated proBNP. Aminotransferases, BUN, creatinine, clotting times, and ferritin were found within normal limits.

The patients' average stay in intensive care was 10 days and there was no mortality.

4. Discussion

This case report, showed that gastrointestinal symptoms and surgical abdomen are manifestations of pediatric patients who develop MIS-C as a consequence of SARS CoV2 infection.

By the end of May 2021, the cases of SARS CoV-2 in the region of Huila continued to increase; 3846 were reported, representing 6.4% of the total positive population and by the date of submission of this paper, the number of cases was already close to 6000, a situation showing their rise and the chance of appearance of MIS-C cases, which increase after 4–6 weeks of the peaks presented in the adult population.

It has been reported that approximately 10–30% of cases of MIS-C can mimic symptoms of appendicitis or acute peritonitis, in this report 23% of a 34-patient cohort with MIS-C was documented [16]. Gastrointestinal manifestations are frequent and of very varied presentation [8,11]. Between 95% and all of the patients with this entity have abdominal pain, vomiting or diarrhea [11]. Comparing gastrointestinal manifestations in adults with SARS CoV-2 infection, they are present in less than 15%, in children between 10 and 20% and in children or adolescents with a diagnosis of MIS-C, between 80 and 100% [2,8,17]. In the study by Miller et al., 84.1% had gastrointestinal symptoms (abdominal pain, vomiting and diarrhea), and 100% of the children under study had fever (N: 44), which is very similar to that described by Shema et al., in a description of 35 patients where 86% presented gastrointestinal involvement. (17.18).

In studies by Blumfield, Shema, Espiñeira et al. imaging findings (abdominal ultrasound, abdominal computed tomography) of patients with MIS-C were analyzed. They found varied findings, but in relation to appendicular pathology, it was reported an increase in mesenteric fat and lymphadenopathy in the right iliac fossa, thickening of the ileal wall and colon. This fact made it difficult to

evaluate the cecal appendix [1,18]. Ileal involvement and imaging findings at this level make it more difficult to differentiate MIS-C from an appendicular surgical process [13,18]. In relation to this fact, it was observed that 1 out of 4 patients was overweight/obese, which constitutes another factor leading to a non-accurate diagnosis.

Meyer et al., report four cases of patients with appendicular surgical pathology and concomitant infection by SARS CoV-2 documented by RT-PCR. They were taken to a surgical procedure which allowed to confirm the suspected diagnosis. One of the cases presented a critical evolution explained by the condition of basic immunodeficiency [14]. In the 8 patients in this series, none had a medical or surgical history other than the nutritional diagnosis. In 3 of the 8 patients (37.5%), the infection was concomitant and the rest of them had past infection documented by positive serological tests.

Tullie et al., in the United Kingdom, in a 8-day period, report 8 patients with “atypical appendicitis”. They had fever, abdominal pain, diarrhea and vomiting, and a SARS CoV-2 infection was documented, with highly variable evolutions. Four patients with a severe inflammatory systemic response. One of them required cardiopulmonary bypass therapy. None required abdominal surgical management and there were no mortality cases [6]. In South Africa, 4 patients with acute abdomen symptoms and positive SARS CoV-2 RT-PCR were reported; three required surgical management and had diagnostic criteria for MIS-C, the other patient was managed in a conservative way, all had a favorable evolution. Among the echocardiographic findings of the coronary arteries, one with normal coronary arteries, one with ecorefringent coronary arteries, and one with dilated coronary arteries was documented; an echocardiogram was not reported in one patient [19]. The multisystemic involvement and the torpid evolution of some cases is very similar to that also reported in this series of cases, where the same outcomes were observed and no mortality was reported. Coronary and myocardial involvement is a diagnostic key for MIS-C in conditions where macroscopic surgical findings of edema or appendicular inflammation are documented, since the inflammatory response due to appendicitis can produce clinical and paraclinical symptoms similar to MIS-C but not alteration of the coronary arteries.

The association between MIS-C and acute appendicitis as the pandemic continues is growing stronger as a diagnostic challenge [10, 15]. In some series such as those mentioned above, cases of appendicitis and of MIS-C have been simultaneously documented. In other series, there has been a wrong diagnosis of appendicitis due to suggestive symptoms of surgical abdomen [6,10]. It is important to carefully evaluate each case of MIS-C to identify those that may require operation and avoid unnecessary procedures in those cases that become a clinical challenge [2,3,7,8,16]. Given the evolution of the pandemic, some groups of health professionals have chosen conservative management of suspected cases of acute appendicitis, by administering antibiotics and even home care [14,20]. In other cases, an echocardiogram has been preferred in order to study myocardial function and coronary evaluation, as well as proBNP, D-dimer, and ferritin levels prior to making the decision to operate [2].

5. Conclusion

We present 8 cases of patients with a diagnosis of MIS-C who required abdominal surgical management and treatment in an intensive care unit, with cardiovascular or respiratory support therapies. With the current evolution of the SARS CoV-2 pandemic, the increase in cases of both COVID-19 and MIS-C, a differential diagnosis of the surgical abdomen must be made in order to properly choose the patients who have to undergo a surgical procedure, always based on clinical manifestations, findings on physical examination and in some occasions the diagnostics imagens can guide cases; as some groups of health professionals, we consider cardiovascular markers (Echocardiogram, troponin, D-dimer, proBNP) as key tools for diagnosis.

Patient consent

Consent to publish the serie of cases 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

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

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Appendix

Table A1
Diagnostic Criteria MIS-C

Characteristics/Entity	WHO	CDC
Name	Multisystemic inflammatory Syndrome in children and adolescents with COVID-19	Multisystemic inflammatory Syndrome in children related to COVID-19 disease
Age	0–19 years	<21 years
Fever	Fever ≥ 3 days	Fever >38 °C for ≥ 24 h or subjective fever \geq a 24 h
Clinical Manifestations	And two of the following: non-purulent bilateral conjunctivitis or signs of mucocutaneous inflammation. Hypotension or shock. Cardiac involvement. Evidence of coagulopathy. Acute gastrointestinal involvement and elevation of inflammation markers C-reactive protein, procalcitonin, erythrocyte globular sedimentation rate	Inflammation evidence from lab tests (C-reactive protein, procalcitonin, globular sedimentation rate). Clinically serious disease requiring hospitalization with multisystemic involvement of organs (≥ 2) (cardiac, renal, respiratory, hematological, gastrointestinal, dermatological or neurological).
Exclusion Criteria	Bacterial sepsis, staphylococcus or streptococcal toxic shock	Alternative diagnosis that explains multisystemic involvement.
Infection Evidence	Evidence of COVID-19 (RT - PCR, positive antigen or serology) or probable physical contact with patients with COVID-19/COVID-19 patients.	SARS-CoV-2 infection diagnosed through RT-PCR, serology or antigen or exposure to COVID-19 within 4 weeks prior to the onset of symptoms.

Table A2

Clinical and demographic characteristics of patients with MIS-C.

Patient	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Total 8
Sex	F	F	F	M	F	M	M	F	F 62.5%
age (months)	120	120	169	191	53	60	103	79	112 (9.5 years)
Abdominal Pain	Si	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100%
Vomit	Si	Yes	No	Yes	Yes	Yes	Yes	Yes	87.5%
Diarrhea	Si	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100%
Fever	Si	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100%
Rash	Si	Yes	Yes	No	No	Yes	Yes	No	62.5%
Conjunctivitis	No	No	Yes	No	No	No	Yes	No	25%
Chock	Si	Yes	Yes	Yes	No	Yes	Yes	Yes	87.5%
Medical History	No	No	No	No	No	No	No	No	0%
Overweight-Obesity	No	No	No	Yes	Yes	No	No	No	25%
RT PCR SARS CoV-2	+	-	-	+	NA	-	NA	+	Positive 37.5%
SARS CoV-2 Antigen	NA	NA	-	-	+	-	-	-	Positive 12.5%
IgG SARS CoV-2	-	-	+	+	NA	-	+	NR	Positive 37.5%
IgM SARS CoV-2	-	+	-	-	NA	+	-	NR	Positive 25%
Diagnostic imaging	Abdominal ultrasound	Abdominal ultrasound	Abdominal ultrasound	Abdominal ultrasound	Unrealized	Unrealized	Unrealized	Abdominal ultrasound	
Imaging findings	Normal.	edema of the intestinal walls, absence of peristalsis.	dilated appendix, aperistaltic, non compressible	Normal	-	-	-	Normal	
Surgical Finding	Normal appendix	Normal appendix	Cecal appendix slightly edematous. Hardening of the last 10 cm of ileum with undamaged serosa.	Cecal edematous appendix	Appendicular plastron, perforated appendix, cecum terminal ileum and/epiploon plastron + pelvic abscess.	Edematous appendix.	Edematous Appendix.	Perforated retro ileal appendix with large pelvic abscess.	
Pathological Finding	No information	No information	Incipient acute appendicitis	Incipient acute appendicitis	Severe acute appendicitis	Reactive follicular hyperplasia	No information	No information	
Echocardiogram EF/FS	68/37	67/33	65/36	67/37	62/33	52/26	60/25	66/34	Average FEVI 63% Average FA 32%
Coronary Involvement	No	No	Hyperrefringence	No	Dilatation Z Score 2-2.4	Aneurysm Z Score 5-9.9	Hiyerrefringence	Dilatation Z Score 2-2.4	Coronary abnormality 62.5%
Inotropic Support	Yes	Yes	Yes	Yes	No	Yes	No	Yes	75%
Immunoglobulin	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100%
Steroid	No	No	No	Yes	No	Yes	No	No	25%
ASA	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	87.5%
Antibiotic	Piperacillin tazobactam.	Piperacillin tazobactam.	Piperacillin tazobactam.	Piperacillin tazobactam.	Ampicilin sulbactam.	Piperacillin tazobactam.	Piperacillin tazobactam	Piperacillin tazobactam.	100%
Days of stay at PICU	10	13	15	11	10	12	3	7	Average 10 days
Final Condition	Alive	Alive	Alive	Alive	Alive	Alive	Alive	Alive	Mortality 0%

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