Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Journal of Pediatric Surgery Case Reports 69 (2021) 101838

Contents lists available at ScienceDirect

Journal of Pediatric Surgery Case Reports

journal homepage: http://www.elsevier.com/locate/epsc

Multisystem inflammatory syndrome in children. An emerging clinical challenge for pediatric surgeons in the COVID 19 era

Francesco Valitutti [a,b,1], Alessandra Verde [c,1], Angela Pepe [d,1], Eduardo Sorrentino [d], Deborah Veneruso [d], Giusy Ranucci [e], Francesca Orlando [e], Augusto Mastrominico [e], Mia Giovanna Grella [f], Claudia Mandato [e,*]

[a] Clinical Pediatrics and Pediatrics, University Hospital "San Giovanni di Dio e Ruggi d'Aragona", Salerno, Italy
[b] EBRIS (European Biomedical Research Institute of Salerno), Salerno, Italy
[c] Department of Traslational Medicine, University of Naples Federico II, Naples, Italy
[d] Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", Pediatrics Section, University of Salerno, Baronissi (Salerno), Italy
[e] Department of Pediatrics, Santobono Pausilipon Children's Hospital, Naples, Italy
[f] Department of Pediatric Surgery, Santobono Pausilipon Children's Hospital, Naples, Italy

ARTICLE INFO

Keywords:
Multisystem inflammatory syndrome in children
COVID-19
Gastrointestinal
Acute abdomen
Emergency surgery

ABSTRACT

Background/purpose: Multisystem inflammatory syndrome in children (MIS-C) is a potentially life-threatening condition occurring 2–6 weeks after Coronavirus disease 2019 (COVID-19) in previously healthy children and adolescents, characterized by clinical and laboratory evidence of multiorgan inflammation. We reported the case of a 6-year-old child presented with acute abdomen and then diagnosed with MIS-C. In addition, to better portray this new entity, we performed a systematic review of MIS-C gastrointestinal features and particularly on those mimicking surgical emergencies.

Methods: We described the clinical presentation, the diagnostic approach and the therapeutic outcomes of our MIS-C patient. Parallel to this, we conducted a systematic literature search using Google Scholar, PubMed, EMBASE, Scopus, focusing on gastrointestinal MIS-C.

Results: Our patient was initially assessed by the surgical team due to his query acute abdomen. Following the diagnosis of MIS-C with myocarditis, intravenous methylprednisolone (2 mg/Kg/day) and intravenous immunoglobulins (2 gr/Kg single infusion) were promptly started, leading to clinical improvement. According to our literature search, patients with MIS-C have a high rate of severe abdominal symptoms resembling surgical emergencies (appendicitis, obstruction, etc.) and a not negligible number of those patients have been surgically explored with variable findings.

Conclusions: We encourage pediatric surgeons in the upcoming months of COVID-19 pandemic to evaluate myocardial function prior to surgical abdominal exploration. In children with query acute abdomen, MIS-C should be promptly ruled out in order to avoid unnecessary surgeries that could worsen the already frail outcome of this new syndrome. Nevertheless, it should be considered that MIS-C might well encompass complications (e.g. appendicitis, segmental intestinal ischemia) which need swift surgical treatment.

1. Introduction

Multisystem Inflammatory Syndrome in Children (MIS-C) related to SARS-CoV-2 has been increasingly reported. It could be a life-threatening condition occurring 2–6 weeks after Coronavirus disease 2019 (COVID-19), in previously healthy children and adolescents. It is characterized by fever, laboratory evidence of inflammation (including increased ferritin and IL-6) and clinically severe illness requiring hospitalization with multisystem (>2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological); moreover, no alternative plausible diagnoses should be accountable and somewhat marker for current or recent SARS-CoV-2 infection should be present (RT-PCR, serology or antigen test) or COVID-19 exposure should fall within the 4 weeks prior to the onset of

* Corresponding author. Department of Pediatrics, Santobono-Pausilipon Children's Hospital, Via Mario Fiore, 6, 80129, Naples, Italy.
E-mail address: cla.mandato@gmail.com (C. Mandato).
[1] These three authors equally contributed to this manuscript.

https://doi.org/10.1016/j.epsc.2021.101838
Received 13 February 2021; Accepted 6 March 2021
Available online 8 April 2021

Table 1
Case definition for Multisystem Inflammatory Syndrome in Children (MIS-C) according to Center for Disease Control (CDC) criteria

1) An individual aged < 21 years with:
2) Clinical criteria:
- Fever > 38C° for ≥ 24 hours, or report of subjective fever lasting ≥ 24 hours AND
- Severe illness necessitating hospitalization AND
- Two or more organ involvement (i.e., cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic, neurological)
3) Evidence of inflammation:
- One or more of the following: an elevated CRP, ESR, fibrinogen, procalcitonin, D-dimer, ferritin, LDH, or IL-6; elevated neutrophils, reduced lymphocytes; low albumin
4) Laboratory or epidemiologic evidence of SARS-CoV-2 infection:
- Positive for current or recent SARS-COV2 infection by RT-PCR, serology or antigen test;
- Exposure to a suspected or confirmed COVID-19 case within the 4 weeks prior to the onset of symptoms.
5) No alternative plausible diagnoses

symptoms (Table 1) [1,2].

Initially, MIS-C was considered as Kawasaki-like because some clinical findings were reminiscent of Kawasaki's disease (KD) [3]. However, current data evidence some difference between these two conditions, such as the age of presentation: the majority of children with KD present before 5 years of age whereas MIS-C affects older children, with a mean age of 8 years [4].

Gastrointestinal symptoms are the most common clinical manifestations of MIS-C (87% of children), followed by muco-cutaneous (73%), cardiovascular (71%), respiratory (47%) and neurologic symptoms in 22% [5].

Abdominal pain, vomiting and diarrhea are particularly common and prominent, with the presentation in some children mimicking acute abdomen. Some children have been noted to have mesenteric adenitis, terminal ileitis and/or colitis on abdominal imaging [6–8]. An increasing number of children referred for suspected appendicitis or acute abdomen are subsequently diagnosed as MIS-C, often after undergoing surgery or after needing intensive care [9,10]. Cardiac involvement includes ventricular dysfunction, coronary artery dilation

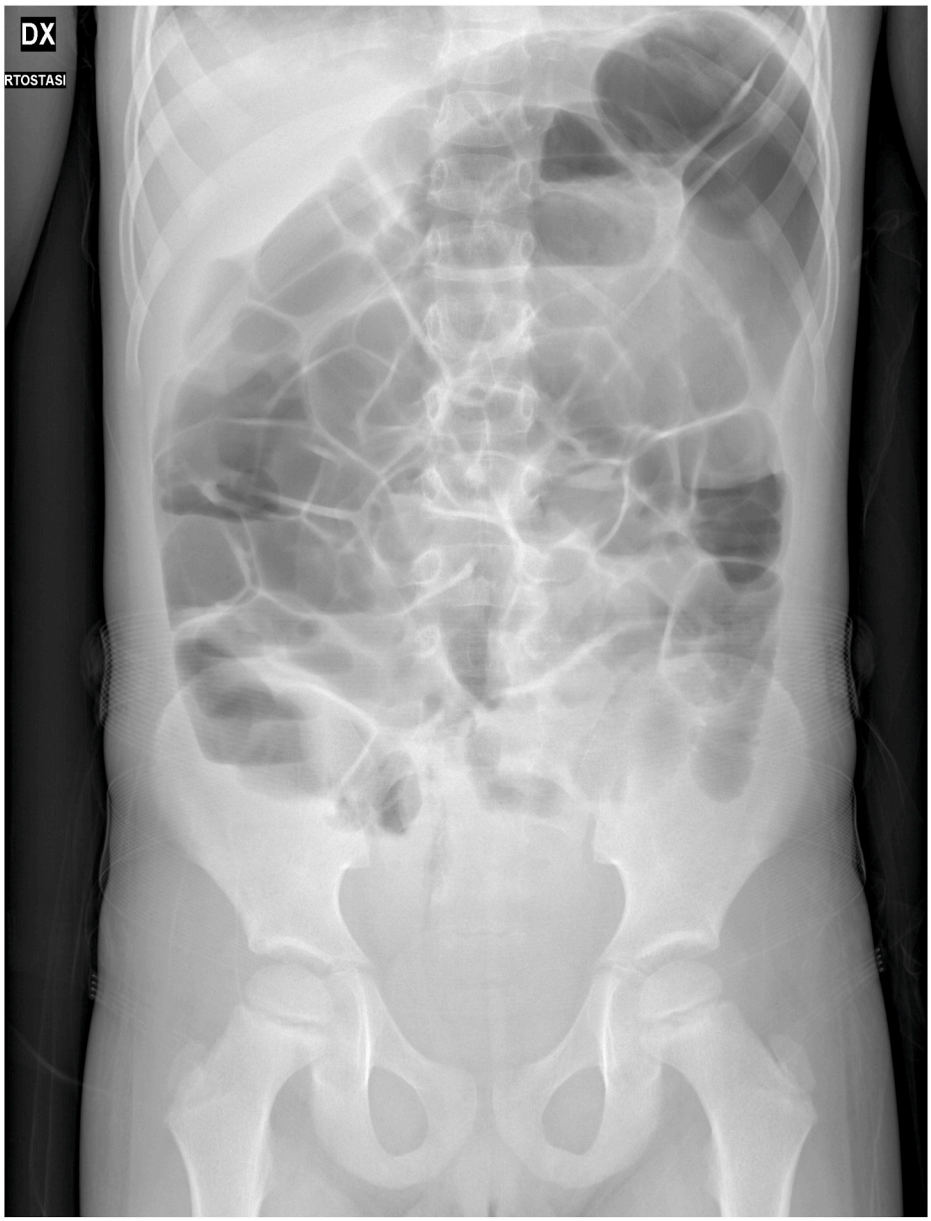


Fig. 1. **1A**. X-Ray showing marked bowel distension due to paralytic ileus; **1B**: US showing free fluid in the pelvis (appendix not visible).

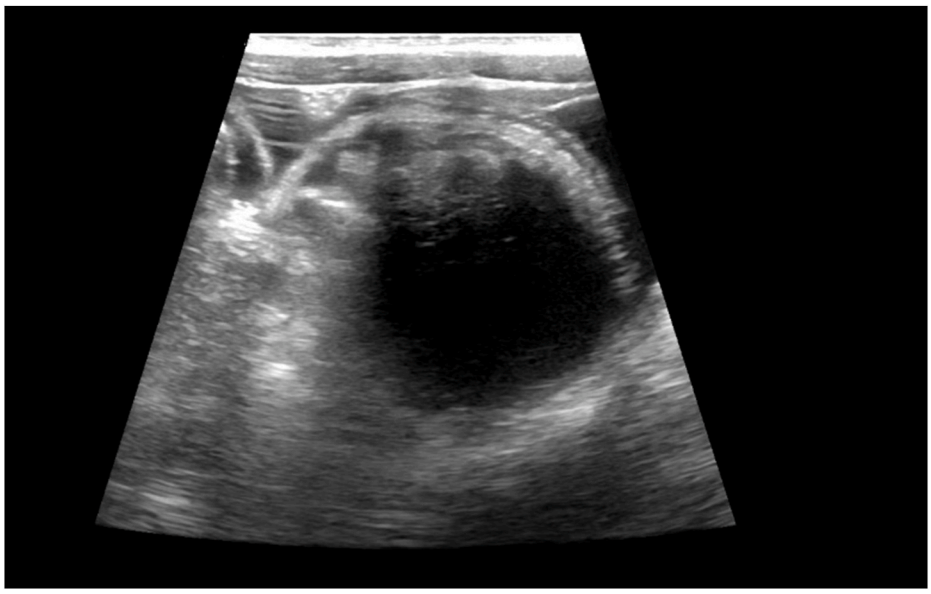


Fig. 1. (*continued*).

or aneurysm, and arrhythmias [11].

Coronary arteries may not be frequently affected in the acute phase and in the early follow-up period of MIS-C. The major finding during the acute phase of MIS-C is a myocarditis-like picture, which may remain subtle and subclinical [12].

Severe pulmonary involvement (e.g. acute respiratory distress syndrome) is rather uncommon; however, when present, respiratory symptoms (tachypnea, dyspnea) are most often due to severe shock [13, 14].

Neurocognitive symptoms are also frequent and may include headache, lethargy, confusion or irritability. A minority of patients presents with more severe neurologic manifestations, including encephalopathy, seizures, coma, meningoencephalitis, muscle weakness and brainstem/cerebellar signs [15].

Herein we describe a new case of MIS-C presenting as acute abdomen and we outline a systematic review of the available literature on abdominal features of this condition.

The practical aim of this work is specifically to highlight MIS-C presenting as acute abdomen, a truly diagnostic and therapeutic dilemma for both pediatric surgeons and pediatric emergency physicians in the COVID-19 era.

LIST OF ABBREVIATION: MIS-C: Multisystem inflammatory syndrome in children; COVID-19: Coronavirus disease 2019; RT-PCR: Reverse transcriptase-polymerase chain reaction; KD: Kawasaki's disease; pAMY: pancreatic amylase; LDH: Lactate dehydrogenase; CPK: creatine phosphokinase; CDC: Centers for Disease Control; BNP: B Natriuretic Peptide; IL-6: interleukin 6.

2. Case presentation

We report the case of a 6-year-old child who was admitted to a secondary-care hospital for fever (up to 40 °C) lasting for five days and intermittent diarrhea. At admission he was pale, with palmar hyperemia; he presented regular cardio-respiratory activity, tense and painful abdomen, with signs of defense in the lower right quadrant; no lymphadenopathy was detected. Sars-Cov-2 testing through both antigenic and molecular nasopharyngeal swab resulted negative. Laboratory tests showed white blood cell count 7850/μL (neutrophils 83%, lymphocytes 10.6%), Hb 11.1 g/dl, platelets 114000/μL, Na+ 126 mEq/L, K+ 3.5 mEq/L, procalcitonin 14.6 ng/mL, C-reactive protein 16.10 mg/dl, fibrinogen 518 mg/dl, albumin 3.5 g/dl, liver function tests were within normal range. Anti- Sars-Cov-2 IgG antibodies were found positive. Ultrasonography evaluation of the abdomen highlighted free pelvic fluid and a non-visible appendix; a plain X-ray showed multiple hydro-aerial levels. This imaging, combined to clinical features and increased inflammatory indices, left the query appendicitis unsolved (Fig. 1A and B).

Surgical consult suggested to prescribe i.v. Ceftazidime, Amikacin and Metronidazole along with watchful monitoring. Given his clinical worsening, a CT scan was performed, showing gas distension of the small bowel and free pelvic fluid; incidentally, pleural and pericardial effusions were found at once. The ECG showed an inversion of T wave. A cardiac ultrasound revealed a slight reduction in the ejection fraction (52%); all coronaries had normal diameter. Testing for cardiac cytolysis enzyme revealed increasing Troponin (278 ng/L), increased B-Natriuretic peptide (935 pg/ml) but normal LDH (551 IU/L) and CPK-mb (3.9 ng/ml). Therefore, MIS-C was highly suspicious and he underwent medical treatment with Methylprednisolone (2 mg/Kg/day) and intravenous immunoglobulins (2 gr/Kg single infusion), on the basis of reported guideline [1], with progressive clinical and biochemical improvement. Laboratory tests over time were summarized in Fig. 2.

Although the clinical condition improved and cardiac function fully restored, he presented a persistent tense abdomen and weak peristalsis. Due to the lack of bowel movements and feeding intolerance, he received parenteral nutrition for 7 days. On day 8, we observed transient elevation of pancreatic enzymes (pAMY 192 IU/L lipase 474 IU/L). Liver and renal function remained within the normal range. As D-dimer increased (2311 ng/ml), he was started on subcutaneous Enoxaparin. After day 12 of hospital stay, the patient was able to fully tolerate oral feeding and was discharged with aspirin (3 mg/kg/day) and oral Prednisone (2 mg/kg/day) then tapered in 15 days. Two weeks after discharge laboratory parameters, ECG, echocardiography and abdomen ultrasound were normal.

Serum IL-6 was tested on serum samples collected at entry and after treatment (297.4 pg/ml and 3.42 pg/ml, respectively; reference range 5.3–7.5 pg/ml).

3. Search strategy and selection criteria

The literature research was conducted from November 27 to January 27 on Google Scholar, Pub Med, EMBASE, Scopus using key-words as follows (Table 2):MIS-C; PIMS; Multisystem inflammatory syndrome in children; pediatric inflammatory multisystem syndrome; cardiac; hearth; cardiovascular; gastrointestinal; bowel; liver; pancreas.

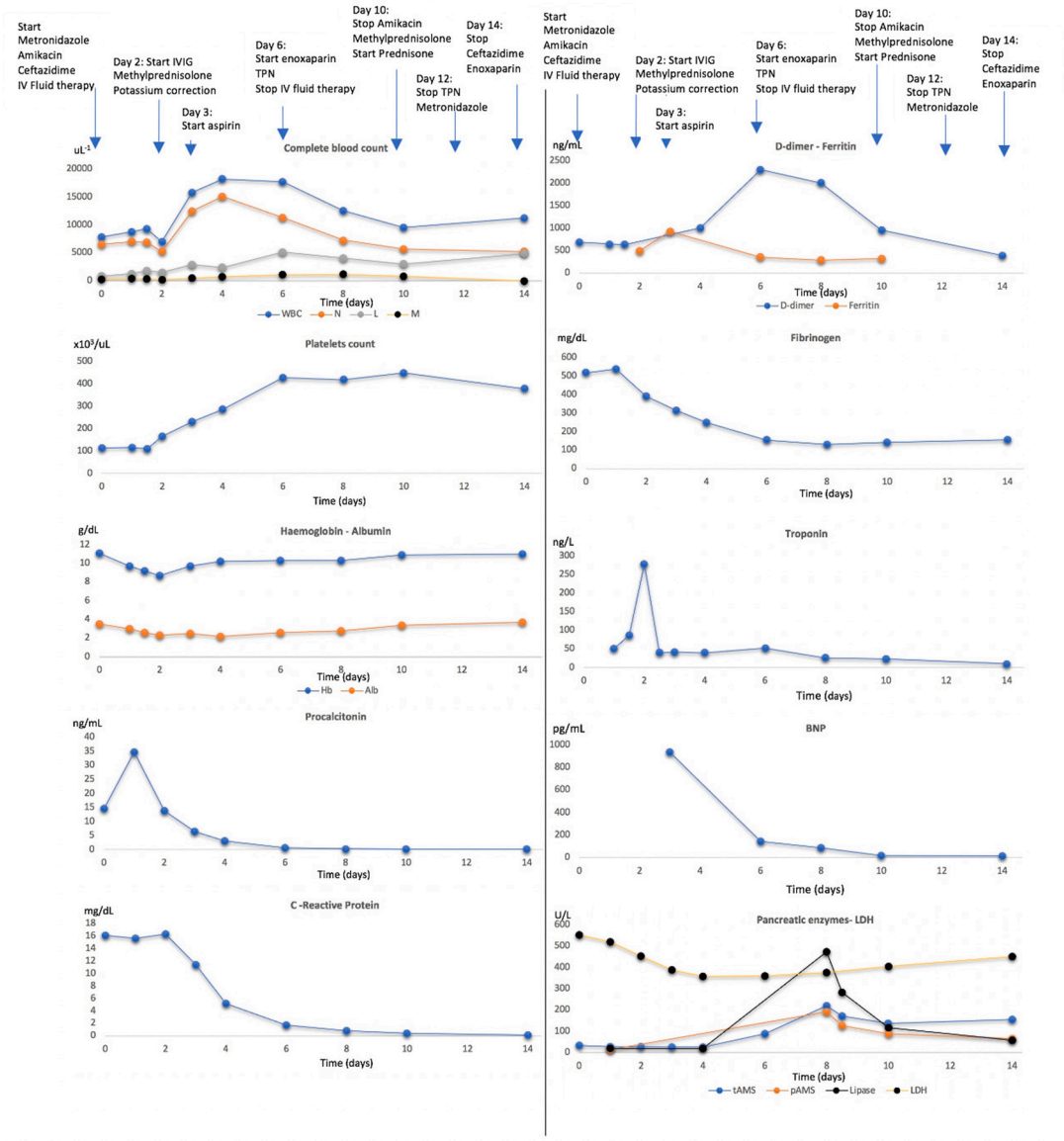


Fig. 2. Biochemical parameters in response to supportive therapies. TPN: total parenteral nutrition. IV: intravenous.

4. Results

A total of 109 articles was retrieved from two authors blinded search, of which eleven were duplicate. Forty-eight were excluded as they were reviews, adult studies (>18 years), guidelines, commentaries, letters, morbidity/mortality report, case-series already reported in another paper included. A final set of 50 articles were suitable for the scope of our review.

Main clinical features of MIS-C reported patients are summarized (Table 3).

When focusing on severe abdominal manifestations, we found nine patients affected by MIS-C who underwent exploratory laparotomies: two children with a healthy appendix as finding ("pseudo appendicular syndrome") [16,17], one with aseptic peritonitis [18], four with appendicitis [19] and two with mesenteric lymphadenitis [20]. Appendicitis was initially suspected in roughly 5–30% [16,18,20–24] of the reviewed case series and in four case reports [9,17,25,26]. Three patients underwent intestinal resection with re-anastomosis due to segmental inflammation with necrosis of terminal ileum [9,17,27].

When considering imaging studies, ileitis or colitis were present approximately in 4–28% of cases [6,7,13,23,27–31]. Moreover, a diagnosis of mesenteric adenitis in MIS-C has been accounted by 8 case-series, with a prevalence of 9–20% of the abdominal imaging studies [6,8,13,16,23,27,31,32]. In addition, the latter condition has been also described in six recent case-reports from different geographic areas [9,25,26,30,33,34]: notably, in one of those patients mesenteric lymphadenitis was even confirmed on surgical specimens by pathologists [9].

Vomiting and diarrhea were common presenting features, respectively in 23% and 21% of patients from the available literature.

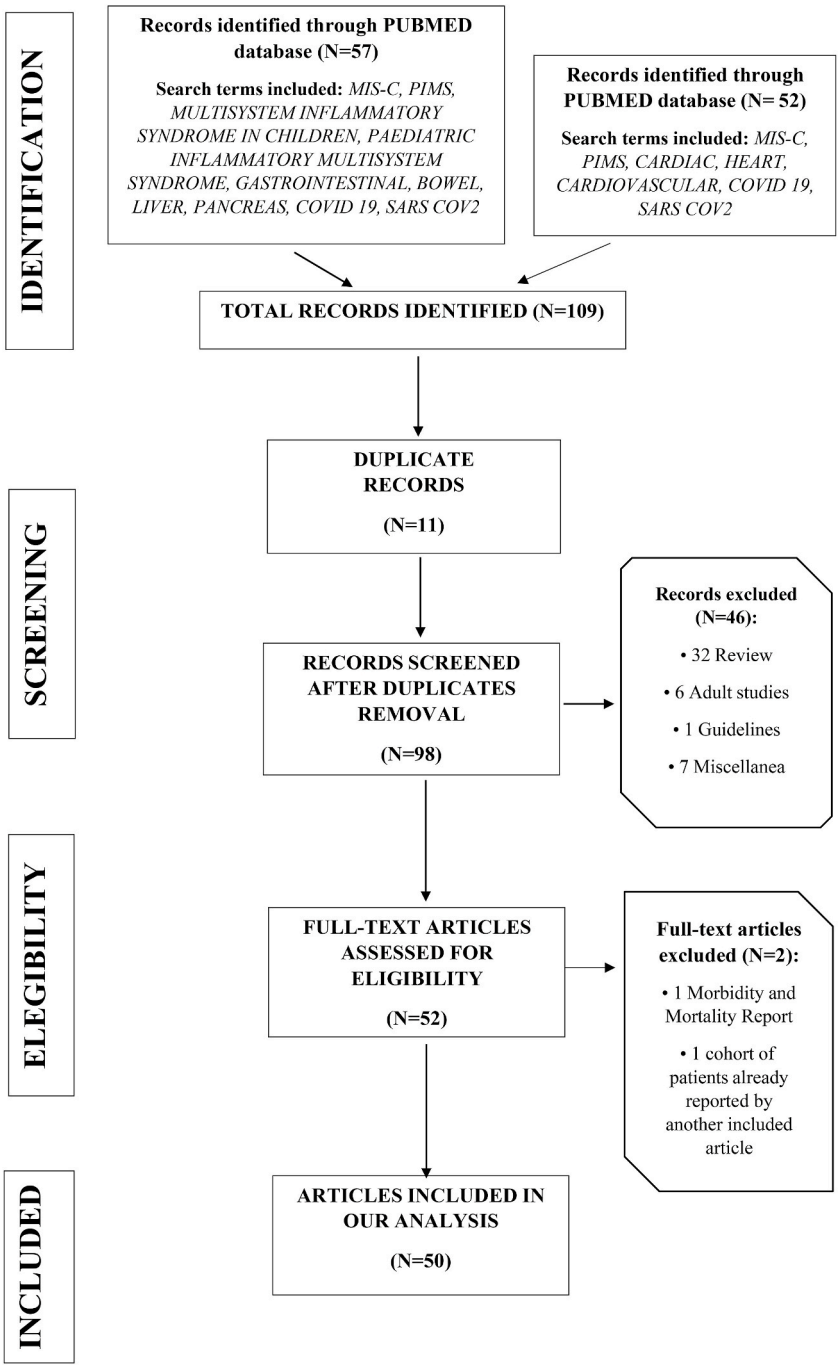
Albeit predominant in our patient, intestinal occlusion was far less common and has been reported in 3 other patients so far [27,30,35].

5. Discussion

The impact of COVID-19 on pediatric population can be considered relatively milder than adults [36]. Furthermore, the concern of contracting Covid-19, stay-at-home orders and population lockdowns have brought to a massive decrease of hospital accesses for children [37]. Notwithstanding this, the fear of SARS-CoV-2 has often delayed pediatric consultations, thus leading to worse clinical outcomes [38].

In this epidemiological framework, an increasing number of children

Table 2
Flow diagram regarding study selection.



has been described with a severe inflammatory disease characterized by fever, hyperinflammation and multiorgan involvement as short-medium term consequence of Sars-Cov2 infection, namely MIS-C. It is important to note that this newly recognized syndrome is most frequently post-infectious (related to an immune dysregulation induced by the virus, i.e. molecular mimicry) rather than related to acute infection [39].

According to CDC criteria [2], our patient could be fully labeled as MIS-C with acute abdomen and early myocarditis.

In this review of the literature, we summarized the features of MIS-C with a special focus on gastrointestinal involvement, thus addressing the need for an appropriate differential diagnosis both in the Emergency Room and during the early stages of hospital stay.

Quite surprisingly, in fact, patients with MIS-C have a high rate of gastrointestinal complaints.

Several authors reported acute abdomen presentation in a not negligible number of patients. Our systematic review of literature evidenced acute abdomen presentation up to 30% [16,18,20–24]. It is attractive to speculate that vascular damage could probably play a role as well with this regard. Indeed, Khesrani et al. reported a case of ischemic lesions complicating MIS-C syndrome and formulated the hypothesis of an underlying severe intestinal vasculitis [17].

A case report by Cazzaniga et al. described a child with KD complicated by the onset of paralytic ileus: this patient also resulted positive for SARS-COV-2 and his X-ray showed ileocolic meteorism with diffuse air-

Table 3
Review of the literature.
[41]; [42]; [43]; [44]; [45]; [46]; [47]; [48]; [49]; [50]; [51]; [52]; [53]; [54]; [55]; [56]; [57]; [58]; [59]; [60]; [61]; [62]; [63].

				HEART							GASTROINTESTINAL					
				ECHOCARDIOGRAM ALTERATION							GI SYMPTOMPS				LIVER	BOWEL
AUTHOR *Journal - Month* Publication month (2020)	Country	N of patients with MIS-C	Demographics Male/Median age	Coronary involvement	↓EF	Valvular involvement	Pericardium	EKG alteration	↑ Troponin	↑ BNP	Abdominal pain	Diarrhea	Vomiting	Abdominal pain and/or diarrhea and/or vomiting N.O.S.	↑ ALT	Imaging alteration
MINOCHA et al. [56] *Clin Pediatr (Phila)* - Sep	USA	33	19 M / 2.8 ys	2 (6%)	4 (13%)	4 (13%)	1 (3%)	16 (48%)	7 (21%)	12 (36%)	10 (30%)	12 (36%)	11 (33%)	-	U	U
MAMISHI et al. [29] *Epidemiol Infect* - Aug	Iran	45	24 M / 7 ys	14 (31%)	N/A	U	1 (2%)	U	N/A	U	26 (58)%	16 (36%)	23 (51%)	-	N/A	US: Ileitis 2 (4%)
MORPARIA et al. [23] *Pediatr Infect Dis J* - Dec	USA	7*	5 M / 6 ys	U	1/1 (100%)	U	U	U	U	U	6/7 (86%)	3/7 (43%)	5/7 (71%)	-	6/7 (86%)	US: Hepatomegaly 5 (71%), gallbladder wall thickening 3 (42%), mesenteric lymphadenopathy 3(14%), acute appendicitis 1 (14%) CT 3/7: mesenteric lymphadenopathy 2 (67%), ileitis 2 (67%)
GERALL et al. [25] *Ann Surg* -Oct	USA	2	2 F / 7 ys	U	U	U	U	U	U	U	2 (100%)	2 (100%)	2 (100%)	-	U	Abdominal Ultrasound 2/2: cecum and ileum thickening 1 (50%), enlargement of the appendix 1 (50%); ovarian cyst and ascites 1 (50%) MRI 1/2: Normal appendix, mesenteric inflammation
ORLANSKI-MEYER et al. [57] *J Pediatric Infect Dis Soc* - Nov	Israel	1	1 F / 2 mo	N	N	Yes	Yes	N	U	Yes	Yes	Yes	Yes	-	Yes	US: Stomach and intestinal edema.
JACKSON et al. [9] *Cureus* - Sep	China	1	1 M / 9 ys	N	N	N	N	N	U	U	Yes	U	Yes	-	U	CT: Right colon thickening
ALAMEER et al. [33] *Cureus* - Sep	Saudi Arabia	1	1 F/ 13 ys	U	Yes	Yes	Yes	U	Yes	U	Yes	Yes	Yes	-	N	US: mesenteric lymphadenopathy
KHEDRANI et al. [17] *J Pediatr Surg Case Rep* - Aug	Algeria	1	1 F / 9 ys	U	U	U	U	U	Yes	U	Yes	Yes	Yes	-	U	US: Swollen appendix, ischemic bowel
STEVENS et al. [58] *J Pediatr Gastroenterol Nutr* - Jul	USA	1	1 F / 10 ys	N	Yes	Yes	N	U	U	U	Yes	Yes	Yes	-	Yes	CT: compatible with acute pancreatitis
RAUF et al. [59] Indian J Pediatr - Sep	India	1	1 M / 5 ys	N	Yes	U	U	U	Yes	Yes	Yes	Yes	U	-	Yes	U
GREENE et al. [60] *Am J Emerg Med* - Jun	USA	1	1 F / 11 ys	N	Yes	U	U	N	Yes	Yes	Yes	N	U	-	U	U
KAUSHIK et al. [30] *Perfusion* - Sep	USA	1	1 M / 5 ys	N	Yes	U	U	U	Yes	Yes	Yes	U	Yes	-	N	X-ray: Non-obstructive distended bowel loop pattern CT: Multiple fluidfilled small bowel loops and concern for mesenteric adenitis versus enteritis
VARI et al. [34] *Prog Pediatr Cardiol* - Sep	USA	1	1 M / 14 ys	Yes	Yes	Yes	U	N	Yes	Yes	Yes	Yes	U	-	U	CT: Distal ileum thickening, diffuse lymphadenopathy
MARVANDI et al. [61] *Cureus* - Oct	USA	1	1 M / 16 mo	N	N	Yes	U	Yes	N	Yes	U	Yes	U	-	N	U
MEREDITH et al. [62] *J Crohns Colitis* - Sep	UK	1	1 F / 10 ys	U	U	U	U	N	N	U	Yes	Yes	U	-	N	Chest X-ray, whole body magnetic resonance imaging, pelvic and abdominal ultrasounds: No abnormalities
LEE et al. [26] *J Korean Med Sci*- Jun 2021	Korea	1	1M/ 12 ys	N	N	Yes	N	U	N	U	Yes	Yes	Yes	-	N	Abdominal X-Ray: no definite abnormality CT: mesenteric lymphadenitis
ALSABRI et al. [35] *Cureus* - Nov 2020	USA	1	1 M/ 13ys	U	Yes	Yes	U	Yes	Yes	Yes	Yes	N	Yes	-	U	Abdominal X-Ray: multiple dilated and air-filled loops of small bowel CT abdomen: dilation of jejunum and ileum without a transition point
TOTAL		1487	920 M (62%)	231 (16%)	482 (32%)	106 (7%)	255 (17%)	234 (16%)	466 (31%)	388 (26%)	376 (25%)	311 (21%)	338 (23%)	402 (27%)	173 (12%)	Patients with imaging suggestive of intestinal occlusion: 3 (0.2%) ‡

CHEUNG et al. [28] * EKG (16/17): nonspecific ST/T-wave abnormalities (63%), attenuated QRS voltage (6,3%), dysrhythmias (premature ventricular contractions, nonsustained ventricular tachycardia, and sinus bradycardia) (19%).
CHOI et al. [53] * First degree AVB 6 (19%), EBBB 1 (3%), prolonged QTc 4 (13%), ectopic atrial rhythm 1 (3%), ST modification 3 (9%),T inversion 5 (16%), non specific ST and/or T abnormalities 14 (44%), nonspecific intraventricular conduction delay or right ventricular conduction delay (16%), right axis deviation (16%), intermittent premature ventricular complexes (3%).

MORPARIA et al. [23] * Number of patients who performed abdominal imaging and whose data are explicit. Total patients = 23.

RIOLLANO CRUZ et al. [63]* ↑ Troponin or BNP 13 (87%)

MILLER et al. [32] *abnormalities on echocardiogram or dysrhythmia 22 (50%)

‡ SAHN et al [27] (CT: marked circumferential thickening and luminal narrowing), KAUSHIK et al. [30] (X-Ray: Non-obstructive distended bowel loop pattern), ALSABRI et al. [35] (Abdominal X-Ray: multiple dilated and air-filled loops of small bowel)

N/A = Not applicable
U = Unknown
N = No/Normal
N.O.S = Not otherwise specified
CT = Computed Tomography
ys = years
mo = months
BNP = Brain Natriuretic Peptide
ALT = Alanine aminotransferase
EKG = Electrocardiogram
EF = Ejection fraction
US = Ultrasound
MRI = Magnetic Resonance Imaging

				HEART							GASTROINTESTINAL					
				ECHOCARDIOGRAM ALTERATION							GI SYMPTOMPS				LIVER	BOWEL
AUTHOR *Journal - Month* Publication month (2020)	Country	N of patients with MIS-C	Demographics Male/Median age	Coronary involvement	↓EF	Valvular involvement	Pericardium	EKG alteration	↑ Troponin	↑ BNP	Abdominal pain	Diarrhea	Vomiting	Abdominal pain and/or diarrhea and/or vomiting N.O.S.	↑ ALT	Imaging alteration
MEYER et al. [19] *J Pediatr Surg Case Rep* - Nov	Spain	4	3 M / 13.5 ys	U	U	U	U	U	U	U	4 (100%)	1 (25%)	4 (100%)	-	1 (25%)	CT: Acute appendicitis without perforation or abscess (100%)
GARCIA SALIDO et al. [41] *Crit Care* - Nov	Spain	45	39 M / 9.4 ys	3 (7%)	22 (49%)	U	U	U	N/A	N/A	40 (91%)	30 (67%)	32 (71%)	-	11 (24%)	U
FERNANDES et al. [14] *J Pediatr* - Nov	USA	69	42 M / 7 ys	N	12 (17%)	U	U	U	N/A	45/58 (78%)	26 (38%)	29 (42%)	32 (46%)	-	N/A	U
LIMA-SETTA et al. [13] *J Pediatr* - Nov	Brazil	56	39 M / 6.2 ys	9/34 (27%)	9/34 (27%)	U	17/34 (30%)	6 (11%)	27 (53%)	42 (75%)	30 (54%)	30 (54%)	21 (38%)	-	N/A	Radiographic imaging: Enteritis 3 (5%), lymphadenopathy 5 (9%)
SHAHBAZNEJAD et al. [16] *BMC Pediatr* - Nov	Iran	10	6 M / 5.37 ± 3.9 ys (mean age)	3 (30%)	3 (30%)	8 (80%)	U	U	2/2 (100%)	U	7 (70%)	6 (60%)	5 (50%)	-	2 (20%)	US: Fluid in abdomen 5 (50%), lymphadenopathy 2 (20%)
GRUBER et al. [24] *Cell* - Sep	USA	9	4 M / 12 ys	5 (67%)	3 (33%)	3 (33%)	U	3 (33%)	7 (78%)	8 (89%)	5 (56%)	3 (33%)	5 (67%)	-	8 (89%)	U
SAHN et al. [27] *J Pediatr Gastroenterol* - Sep	USA	35	22 M / 8.6 ys	U	U	U	U	U	U	U	34 (97%)	34 (97%)	34 (97%)	-	U	US (11/35): Ileal thickening 3 (27%) CT (7/35): Inflammatory bowel changes 6 (86%), terminal ileitis 4 (57%), marked circumferential thickening and luminal narrowing 1 (14%), mesenteric lymphadenopathy 5 (71%)
TORRES et al. [42] *Int J Infect Dis* - Aug	Chile	27	14 M / 6 ys	5/26 (15%)	4/26 (15%)	U	3/26 (12%)	U	N/A	U	17 (63%)	17 (63%)	13 (48%)	-	U	U
PEREIRA et al. [43] *Clinics (Sao Paulo)* - Aug	Brazil	6	5 M / 7.78 ys	2 (30%)	2 (30%)	U	3 (50%)	U	N/A	U	N/A	N/A	N/A	4 (67%)	N/A	U
BLUMFIELD et al. [8] *AJR Am J Roentgenol* - Jul	USA	16	10 M / 9.2±4.9 ys (mean)	4 (25%)	10 (63%)	U	2 (13%)	U	6 (38%)	15 (94%)	11 (69%)	7 (44%)	12 (75%)	-	15 (94%)	X-Ray/US/CT*: Bowel wall thickening 3 (19%), paucity of bowel gas 3 (19%), bowel dilation 2 (13%), ascites 6 (38%), mesenteric lymphadenopathy 2 (13%)
KEST et al. [44] *Case Rep Pediatr* - Jul	USA	3	1 M / 8 ys	N	3 (100%)	U	1 (33%)	1/1 (100%)	3 (100%)	3 (100%)	2 (67%)	2 (67%)	2 (67%)	-	U	U
FELDSTEIN et al. [45] *N Engl J Med* - Jun	USA	186	115 M / 8.3 ys	15/170 (9%)	EF 30 -55%: 61/170 (36%) EF < 30%: 9/170 (5%)	U	48/170 (28%)	22 (12%)	77/153 (50%)	94/128 (73%)	N/A	N/A	N/A	171 (92%)	N/A	U
MILLER et al. [32] *Gastroenterology* - Oct	USA	44	20 M / 7.3 ys	N/A*	N/A*	N/A*	N/A*	N/A*	U	U	33 (75%)	18 (40%)	25 (57%)	-	23 (52%)	MRI 2/44: Ascites 2 (100%) terminal ileum and descending colon thickening 1 (50%) US 12/44: Ascites 4 (33%), mesenteric lymphadenopathy 2 (17%), bowel wall thickening 4 (33%), gallbladder sludge 3 (25%)
CHEUNG et al. [28] *JAMA* - Jun	USA	17	8 M / 8 ys	1 (6%)	11 (65%)	U	8 (47%)	N/A*	14 (82%)	15 (88%)	N/A	N/A	N/A	15 (88%)	N/A	Acute ileocolitis 1 (6%)
TOUBIANA et al. [18] *BMJ* - May	France	21	9 M / 7.9 ys	8 (38%)	16 (76%)	U	U	2/16 (13%)	17/21 (81%)	14/18 (78%)	N/A	N/A	N/A	21 (100%)	13 (62%)	U
BELHADJER et al. [20] *Circulation* - May	France	35	18 M / 10 ys	6 (17%)	EF 30-50%: 25 (72%) EF<30%: 10 (28%)	U	3 (9%)	1 (3%)	35 (100%)	35 (100%)	N/A	N/A	N/A	28 (80%)	U	U
CHIOTOS et al. [7] *J Pediatric Infect Dis Soc*- Jul	USA	6	1 M / 9.5 ys	1 (17%)	4 (67%)	U	U	U	5 (83%)	4 (67%)	N/A	4 (67%)	N/A	5 (83%)	4 (67%)	CT 1/6 : Ileocolitis 1 (100%)
POULETTY et al. [46] *Ann Rheum Dis* - Jun	France	16	8 M / 10 ys	3 (19%)	7 (43%)	U	4 (25%)	U	11/11 (100%)	11/11 (100%)	N/A	N/A	N/A	13 (81%)	5 (31%)	U
CAPONE et al. [47] *J Pediatr*- Sep	USA	33	20 M / 8.6 ys	16 (48%)	19 (58%)	U	U	U	N/A	N/A	N/A	N/A	N/A	32 (97%)	7 (21%)	U
MORALEDA et al. [48] *Clin Infect Dis* - Jul	Spain	31	18 M / 7.6 ys	3 (10%)	15 (48%)	9 (29%)	6 (19%)	7 (23%)	N/A	N/A	N/A	N/A	N/A	27 (97%)	N/A	U
KHUEN FOONG NG et al. [49] *J Med Virol* - Nov	UK	3	1 M / 16 ys	2 (66%)	1 (33%)	1 (33%)	2 (67%)	U	3 (100%)	3 (100%)	3 (100%)	3 (100%)	3 (100%)	-	2 (67%)	U
RIOLLANO CRUZ et al. [63] *J Med Virol* - Jun	USA	15	7 M / 12 ys	3 (20%)	7 (47%)	11 (73%)	9 (60%)	2 (13%)	N/A*	N/A*	9 (60%)	6 (40%)	12 (80%)	-	N/A	U
ANTUNEZ-MONTES et al. [50] *Pediatr Infect Dis J* - Jun 2021	Latin America	95	52 M / 7 ys	5 (5%)	U	U	4 (4%)	U	U	U	N/A	N/A	N/A	43 (45%)	U	U
RAMCHARAN et al. [51] *Pediatr Cardiol* - Oct	UK	15	11 M / 8.8 ys	14 (93%)	12 (80%)	13 (87%)	8 (53%)	9 (60%)	N/A	N/A	N/A	N/A	N/A	13 (87%)	U	U
WHITTAKER et al. [52] *JAMA* - Jul	UK	58	25 M / 9 ys	8 (14%)	18 (31%)	U	U	4 (7%)	56 (97%)	29 (50%)	31 (53%)	30 (52%)	26 (49%)	-	56 (97%)	U
DUFORT et al. [31] *N Engl J Med* - Jul	USA	99	53 M 0-5 (31) 6-12 (42) 13-20 (26)	9 (9%)	51 (51%)	U	32 (32%)	59 (60%)	N/A	N/A	60 (61%)	49 (49%)	57 (58%)	-	U	US and/or CT (44/99): mesenteric lymphadenopathy 8 (18%), ascitis, pleural effusions or pelvic fluid 16 (36%), inflammation or enlargement of the appendix 2 (5%), enteritis or enterocolitis 3 (7%), bowel-wall thickening 7 (16%), thickfilled bowel loops 4 (9%)
CHOI et al. [53] *Pediatrics* - Nov	USA	32	17 M / 9 ys	U	2 (6%)	U	U	N/A*	N/A	N/A	U	U	U	U	U	U
FELSENSTEIN et al. [21] *J Clin Med* - Oct	UK	29	20 M / 6 ys	15 (52%)	10 (33%)	10 (33%)	8 (26%)	U	12 (41%)	22 (76%)	N/A	N/A	N/A	21 (72%)	12/26 (46%)	7/19 (37%)
DHANALAKSHMI et al. [22] *Indian Pediatr* - Nov	India	19	8 M / 6 ys	3 (16%)	N/A	U	2 (5%)	U	1/6 (5%)	3/4 (16%)	8 (42%)	3 (16%)	6 (32%)	-	5 (26%)	U
THEOCHARIS et al. [54] *Eur Heart J Cardiovasc Imaging* - Aug	UK	20	15 M / 11 ys	N/A	10 (50%)	15 (75%)	2 (10%)	U	U	U	U	U	U	U	U	U
BLUMFIELD, LEVIN [55] *Pediatr Radiol* - Sep	USA	19	10 M / 8 ys	1 (5%)	5 (26%)	U	U	U	3 (16%)	5 (26%)	N/A	N/A	N/A	9 (47%)	U	U
VALVERDE et al. [6] *Circulation* - Nov	EUR	286	194 M / 8.4 ys	69 (24%)	97 (34%)	12-17 (4-6%)	80 (28,%)	100 (35%)	173/187 (93%)	21/22 (95%)	N/A	N/A	N/A	N/A	U	US: Ileitis 14 (9%), colitis 6 (4%), lymphadenopathy 22 (14%)
MATSUBARA et al. [12] *J Am Coll Cardiol* - Oct	USA	28	50 M / 11.4 ys	1 (4%)	12 (43%)	13 (46%)	9 (32%)	U	N/A	N/A	U	U	U	U	U	U

fluid levels, compatible indeed with paralytic ileus associated to intestinal vasculopathy [40]. Nonetheless, it should be noted that this case was not an outcome of our search nor present in Table 3 because classified as KD rather than MIS-C.

In our opinion, for these unclear cases it is definitely valuable a period of watchful monitoring in a hospital setting. Subsequently, if the clinical picture does not improve, a different abdominal imaging might be required. Should patient's clinical status worsen further, an extensive abdominal imaging (MR angiogram preferably or CT angiogram) must be considered, as well as to promptly establish the best treatment and to avoid complications.

Given the high rate of severe abdominal symptoms resembling surgical emergencies (query appendicitis or obstruction) in MIS-C, we encourage pediatric surgeons in the upcoming months to evaluate myocardial function prior to surgical abdominal exploration. Few laboratory and imaging tools should become full part of the initial diagnostic panoply. A preliminary assessment of troponin, BNP, D-Dimer, ferritin and echocardiography are definitely of value to establish a precise differential diagnosis in children with acute abdomen, as it was in our case. Considering the high overlap between gastrointestinal and cardiac involvement in MIS-C, evolution towards cardiogenic shock should not be neglected, especially when avoidable surgery might worsen its already frail outcomes. Nevertheless, it must be acknowledged that several cases of MIS-C do evolve in insidious surgical complications such as appendicitis and vasculopathy-related segmental intestinal infarction. Rather than being ancillary, the role of pediatric surgeons in MIS-C is thus key and so it will be in the months ahead of current pandemic.

In conclusion, the awareness on the high rate of gastrointestinal complaints in MIS-C is definitely an added value for both pediatricians and pediatric surgeons. A multidisciplinary approach is more than desirable for these children, with both team's side-by-side against possible confounders and hazardous complications, always aiming to the best therapeutic outcome.

Author statement

Study conception and design: Francesco Valitutti, Angela Pepe, Claudia Mandato

Data acquisition: Edoardo Sorrentino, Deborah Veneruso, Giusy Ranucci

Analysis and data interpretation: Angela Pepe, Alessandre Verde, Edoardo Sorrentino, Deborah Veneruso, Francesca Orlando, Augusto Mastrominico, Mia Giovanna Grella, Giusy Ranucci

Drafting of the manuscript: Francesco Valitutti, Angela Pepe, Alessandre Verde, Claudia Mandato

Critical revision: Augusto Mastrominico, Mia Giovanna Grella, Francesca Orlando Submit this form with the manuscript.

Funding

The APC for this project was supported by the regional fund POR FESR CAMPANIA 2014-2020 – G58D20000240002.

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.

Declaration of competing interest

All the authors have no interest to disclose.

Acknowledgements

All the authors warmly thank Prof. Pietro Vajro for his expert supervision and fruitful discussion on both patient case and manuscript preparation. The authors thank the regional fund POR FESR CAMPANIA 2014-2020 (G58D20000240002) for the support of the APC.

References

[1] Henderson LA, Canna SW, Friedman KG, et al. American college of rheumatology clinical guidance for pediatric patients with multisystem inflammatory syndrome in children (MIS-C) associated with SARS-CoV-2 and hyperinflammation in COVID-19. Version 2. Arthritis Rheum 2020. https://doi.org/10.1002/art.41616.

[2] Centers for Disease Control and Prevention (CDC). Emergency preparedness and response: health alert network. https://emergency.cdc.gov/han/2020/han00432.asp. [Accessed 31 January 2021].

[3] Henderson LA, Yeung RSM. MIS-C: early lessons from immune profiling. Nat Rev Rheumatol 2020:1–2. https://doi.org/10.1038/s41584-020-00566-y.

[4] Centers for Disease Control and Prevention (CDC). Health department-reported cases of multisystem inflammatory syndrome in children (MIS-C) in the United States. https://www.cdc.gov/mis-c/cases/index.html. [Accessed 31 January 2021].

[5] Abrams JY, Godfred-Cato SE, Oster ME, et al. Multisystem inflammatory syndrome in children associated with severe acute respiratory syndrome coronavirus 2: a systematic review. J Pediatr 2020;226:45–54. https://doi.org/10.1016/j.jpeds.2020.08.003. e1.

[6] Valverde I, Singh Y, Sanchez-de-Toledo J, et al. Acute cardiovascular manifestations in 286 children with multisystem inflammatory syndrome associated with COVID-19 infection in europe. Circulation 2021;143:21–32. https://doi.org/10.1161/CIRCULATIONAHA.120.050065.

[7] Chiotos K, Bassiri H, Behrens EM, et al. Multisystem inflammatory syndrome in children during the coronavirus 2019 pandemic: a case series. J Pediatric Infect Dis Soc 2020;9:393–8. https://doi.org/10.1093/jpids/piaa069.

[8] Blumfield E, Levin TL, Kurian J, et al. Imaging findings in multisystem inflammatory syndrome in children (MIS-C) associated with coronavirus disease (COVID-19). AJR Am J Roentgenol 2020:1–11. https://doi.org/10.2214/AJR.20.24032.

[9] Jackson RJ, Chavarria HD, Hacking SM. A case of multisystem inflammatory syndrome in children mimicking acute appendicitis in a COVID-19 pandemic area. Cureus 2020;12:e10722. https://doi.org/10.7759/cureus.10722.

[10] Tullie L, Ford K, Bisharat M, et al. Gastrointestinal features in children with COVID-19: an observation of varied presentation in eight children. Lancet Child Adolesc Health 2020;4:e19–20. https://doi.org/10.1016/S2352-4642(20)30165-6.

[11] Sperotto F, Friedman KG, Son MBF, et al. Cardiac manifestations in SARS-CoV-2-associated multisystem inflammatory syndrome in children: a comprehensive review and proposed clinical approach. Eur J Pediatr 2021;180:307–22. https://doi.org/10.1007/s00431-020-03766-6.

[12] Matsubara D, Kauffman HL, Wang Y, et al. Echocardiographic findings in pediatric multisystem inflammatory syndrome associated with COVID-19 in the United States. J Am Coll Cardiol 2020;76:1947–61. https://doi.org/10.1016/j.jacc.2020.08.056.

[13] Lima-Setta F, Magalhães-Barbosa MC, Rodrigues-Santos G, et al. Multisystem inflammatory syndrome in children (MIS-C) during SARS-CoV-2 pandemic in Brazil: a multicenter, prospective cohort study. J Pediatr 2020. https://doi.org/10.1016/j.jped.2020.10.008. S0021-7557:30225-4.

[14] Fernandes DM, Oliveira CR, Guerguis S, et al. Severe acute respiratory syndrome coronavirus 2 clinical syndromes and predictors of disease severity in hospitalized children and youth. J Pediatr 2020. https://doi.org/10.1016/j.jpeds.2020.11.016. S0022-3476:31393-31397.

[15] Lin JE, Asfour A, Sewell TB, et al. Neurological issues in children with COVID-19. Neurosci Lett 2020;743:135567.

[16] Shahbaznejad L, Navaeifar MR, Abbaskhanian A, et al. Clinical characteristics of 10 children with a pediatric inflammatory multisystem syndrome associated with COVID-19 in Iran. BMC Pediatr 2020;20:513. https://doi.org/10.1186/s12887-020-02415-z.

[17] Khesrani LS, Chana K, Sadar FZ, et al. Intestinal ischemia secondary to Covid-19. J Pediatr Surg Case Rep 2020;61:101604. https://doi.org/10.1016/j.epsc.2020.101604.

[18] Toubiana J, Poirault C, Corsia A, et al. Kawasaki-like multisystem inflammatory syndrome in children during the covid-19 pandemic in Paris, France: prospective observational study. BMJ 2020;369:m2094. https://doi.org/10.1136/bmj.m2094.

[19] Meyer JS, Robinson G, Moonah S, et al. Acute appendicitis in four children with SARS-CoV-2 infection. J Pediatr Surg Case Rep 2021;64:101734. https://doi.org/10.1016/j.epsc.2020.101734.

[20] Belhadjer Z, Méot M, Bajolle F, et al. Acute heart failure in multisystem inflammatory syndrome in children in the context of global SARS-CoV-2 pandemic. Circulation 2020;142:429–36. https://doi.org/10.1161/CIRCULATIONAHA.120.048360.

[21] Felsenstein S, Willis E, Lythgoe H, et al. Presentation, treatment response and short-term outcomes in paediatric multisystem inflammatory syndrome temporally associated with SARS-CoV-2 (PIMS-TS). J Clin Med 2020;9:3293. https://doi.org/10.3390/jcm9103293.

[22] Dhanalakshmi K, Venkataraman A, Balasubramanian S, et al. Epidemiological and clinical profile of pediatric inflammatory multisystem syndrome - temporally associated with SARS-CoV-2 (PIMS-TS) in Indian children. Indian Pediatr 2020;57:1010–4. https://doi.org/10.1007/s13312-020-2025-1.
[23] Morparia K, Park MJ, Kalyanaraman M, et al. Abdominal imaging findings in critically ill children with multisystem inflammatory syndrome associated with COVID-19. Pediatr Infect Dis J 2020;40:e82–3. https://doi.org/10.1097/INF.0000000000002967.
[24] Gruber C, Patel R, Trachman R, et al. Mapping systemic inflammation and antibody responses in multisystem inflammatory syndrome in children (MIS-C). Cell 2020;183:982–95. https://doi.org/10.1016/j.cell.2020.09.034. e14.
[25] Gerall CD, Duron VP, Griggs CL, et al. Multisystem inflammatory syndrome in children mimicking surgical pathologies: what surgeons need to know about MIS-C. Ann Surg 2020. https://doi.org/10.1097/SLA.0000000000004368.
[26] Lee JH, Han HS, Lee JK. The importance of early recognition, timely management, and the role of healthcare providers in multisystem inflammatory syndrome in children. J Kor Med Sci 2021;36:e17. https://doi.org/10.3346/jkms.2021.36.e17.
[27] Sahn B, Eze OP, Edelman MC, et al. Features of intestinal disease associated with COVID-related multisystem inflammatory syndrome in children. J Pediatr Gastroenterol Nutr 2020. https://doi.org/10.1097/MPG.0000000000002953.
[28] Cheung EW, Zachariah P, Gorelik M, et al. Multisystem inflammatory syndrome related to COVID-19 in previously healthy children and adolescents in New York city. J Am Med Assoc 2020;324:294–6. https://doi.org/10.1001/jama.2020.10374.
[29] Mamishi S, Movahedi Z, Mohammadi M, et al. Multisystem inflammatory syndrome associated with SARS-CoV-2 infection in 45 children: a first report from Iran. Epidemiol Infect 2020;148:e196. https://doi.org/10.1017/S095026882000196X.
[30] Kaushik S, Ahluwalia N, Gangadharan S, et al. ECMO support in SARS-CoV2 multisystem inflammatory syndrome in children in a child. Perfusion 2020. https://doi.org/10.1177/0267659120954386. 267659120954386.
[31] Dufort EM, Koumans EH, Chow EJ, et al. Multisystem inflammatory syndrome in children in New York state. N Engl J Med 2020;383:347–58. https://doi.org/10.1056/NEJMoa2021756.
[32] Miller J, Cantor A, Zachariah P, et al. Gastrointestinal symptoms as a major presentation component of a novel multisystem inflammatory syndrome in children that is related to coronavirus disease 2019: a single center experience of 44 cases. Gastroenterology 2020;159:1571–4. https://doi.org/10.1053/j.gastro.2020.05.079. e2.
[33] Al Ameer HH, AlKadhem SM, Busaleh F, et al. Multisystem inflammatory syndrome in children temporally related to COVID-19: a case report from Saudi arabia. Cureus 2020;12:e10589. https://doi.org/10.7759/cureus.10589.
[34] Vari D, Miller JM, Rellosa N, et al. Severe cardiac dysfunction in a patient with multisystem inflammatory syndrome in children associated with COVID-19: retrospective diagnosis of a puzzling presentation. A case report. Prog Pediatr Cardiol 2020;58:101270. https://doi.org/10.1016/j.ppedcard.2020.101270.
[35] Alsabri M, Sakr M, Qarooni S, et al. COVID-19 infection in a child presenting with functional intestinal obstruction. Cureus 2020;12:e11448. https://doi.org/10.7759/cureus.11448.
[36] Cruz AT, Zeichner SL. COVID-19 in children: initial characterization of the pediatric disease. Pediatrics 2020;145. https://doi.org/10.1542/peds.2020-0834.
[37] Valitutti F, Zenzeri L, Mauro A, et al. Effect of population lockdown on pediatric emergency Room demands in the era of COVID-19. Front Pediatr 2020;8:521. https://doi.org/10.3389/fped.2020.00521.
[38] Lazzerini M, Barbi E, Apicella A, et al. Delayed access or provision of care in Italy resulting from fear of COVID-19. Lancet Child Adolesc Health 2020;4:e10–1. https://doi.org/10.1016/S2352-4642(20)30108-5.
[39] Nakra NA, Blumberg DA, Herrera-Guerra A, et al. Multi-system inflammatory syndrome in children (MIS-C) following SARS-CoV-2 infection: review of clinical presentation, hypothetical pathogenesis, and proposed management. Children 2020;7:69. https://doi.org/10.3390/children7070069.
[40] Cazzaniga M, Baselli LA, Cimaz R, et al. SARS-COV-2 infection and Kawasaki disease: case report of a hitherto unrecognized association. Front Pediatr 2020;8:398. https://doi.org/10.3389/fped.2020.00398.
[41] García-Salido A, de Carlos Vicente JC, Belda Hofheinz S, et al. Severe manifestations of SARS-CoV-2 in children and adolescents: from COVID-19 pneumonia to multisystem inflammatory syndrome: a multicentre study in pediatric intensive care units in Spain. Crit Care 2020;24:666. https://doi.org/10.1186/s13054-020-03332-4.
[42] Torres JP, Izquierdo G, Acuña M, et al. Multisystem inflammatory syndrome in children (MIS-C): report of the clinical and epidemiological characteristics of cases in Santiago de Chile during the SARS-CoV-2 pandemic. Int J Infect Dis 2020;100:75–81. https://doi.org/10.1016/j.ijid.2020.08.062.
[43] Pereira MFB, Litvinov N, Farhat SCL, et al. Severe clinical spectrum with high mortality in pediatric patients with COVID-19 and multisystem inflammatory syndrome. Clinics 2020;75:e2209. https://doi.org/10.6061/clinics/2020/e2209.
[44] Kest H, Kaushik A, DeBruin W, et al. Multisystem inflammatory syndrome in children (MIS-C) associated with 2019 novel coronavirus (SARS-CoV-2) infection. Case Rep Pediatr 2020;2020:8875987. https://doi.org/10.1155/2020/8875987.
[45] Feldstein LR, Rose EB, Horwitz SM, et al. Multisystem inflammatory syndrome in U.S. Children and adolescents. N Engl J Med 2020;383:334–46. https://doi.org/10.1056/NEJMoa2021680.
[46] Pouletty M, Borocco C, Ouldali N, et al. Paediatric multisystem inflammatory syndrome temporally associated with SARS-CoV-2 mimicking Kawasaki disease (Kawa-COVID-19): a multicentre cohort. Ann Rheum Dis 2020;79:999–1006. https://doi.org/10.1136/annrheumdis-2020-217960.
[47] Capone CA, Subramony A, Sweberg T, et al. Characteristics, cardiac involvement, and outcomes of multisystem inflammatory syndrome of childhood associated with severe acute respiratory syndrome coronavirus 2 infection. J Pediatr 2020;224:141–5. https://doi.org/10.1016/j.jpeds.2020.06.044.
[48] Moraleda C, Serna-Pascual M, Soriano-Arandes A, et al. Multi-inflammatory syndrome in children related to SARS-CoV-2 in Spain. Clin Infect Dis 2020. https://doi.org/10.1093/cid/ciaa1042.
[49] Ng KF, Kothari T, Bandi S, et al. COVID-19 multisystem inflammatory syndrome in three teenagers with confirmed SARS-CoV-2 infection. J Med Virol 2020;92:2880–6. https://doi.org/10.1002/jmv.26206.
[50] Antúnez-Montes OY, Escamilla MI, Figueroa-Uribe AF, et al. COVID-19 and multisystem inflammatory syndrome in Latin American children: a multinational study. Pediatr Infect Dis J 2021;40:e1–6. https://doi.org/10.1097/INF.0000000000002949.
[51] Ramcharan T, Nolan O, Lai CY, et al. Paediatric inflammatory multisystem syndrome: temporally associated with SARS-CoV-2 (PIMS-TS): cardiac features, management and short-term outcomes at a UK tertiary paediatric hospital. Pediatr Cardiol 2020;41:1391–401. https://doi.org/10.1007/s00246-020-02391-2.
[52] Whittaker E, Bamford A, Kenny J, et al. Clinical characteristics of 58 children with a pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2. J Am Med Assoc 2020;324:259–69. https://doi.org/10.1001/jama.2020.10369.
[53] Choi NH, Fremed M, Starc T, et al. MIS-C and cardiac conduction abnormalities. Pediatrics 2020;146:e2020009738. https://doi.org/10.1542/peds.2020-009738.
[54] Theocharis P, Wong J, Pushparajah K, et al. Multimodality cardiac evaluation in children and young adults with multisystem inflammation associated with COVID-19. Eur Heart J Cardiovasc Imaging 2020. https://doi.org/10.1093/ehjci/jeaa212.
[55] Blumfield E, Levin TL. COVID-19 in pediatric patients: a case series from the Bronx, NY. Pediatr Radiol 2020;50:1369–74. https://doi.org/10.1007/s00247-020-04782-2.
[56] Minocha PK, Phoon CKL, Verma S, et al. Cardiac findings in pediatric patients with multisystem inflammatory syndrome in children associated with COVID-19. Clin Pediatr 2020. https://doi.org/10.1177/0009922820961771. 9922820961771.
[57] Orlanski-Meyer E, Yogev D, Auerbach A, et al. Multisystem inflammatory syndrome in children associated with SARS-CoV-2 in an 8-week old infant. J Pediatric Infect Dis Soc 2020. https://doi.org/10.1093/jpids/piaa137.
[58] Stevens JP, Brownell JN, Freeman AJ, et al. COVID-19-Associated multisystem inflammatory syndrome in children presenting as acute pancreatitis. J Pediatr Gastroenterol Nutr 2020. https://doi.org/10.1097/MPG.0000000000002860.
[59] Rauf A, Vijayan A, John ST, et al. Multisystem inflammatory syndrome with features of atypical Kawasaki disease during COVID-19 pandemic. Indian J Pediatr 2020;87:745–7. https://doi.org/10.1007/s12098-020-03357-1.
[60] Greene AG, Saleh M, Roseman E, et al. Toxic shock-like syndrome and COVID-19: multisystem inflammatory syndrome in children (MIS-C). Am J Emerg Med 2020;38:2492. https://doi.org/10.1016/j.ajem.2020.05.117. e5-e6.
[61] Makvandi S, Alibrahim O, Abdul-Aziz R, et al. A rare presentation of multi-system inflammatory disease in children associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Cureus 2020;12:e10892. https://doi.org/10.7759/cureus.10892.
[62] Meredith J, Khedim CA, Henderson P, et al. Paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) in a patient receiving infliximab therapy for inflammatory bowel disease. J Crohns Colitis 2020. https://doi.org/10.1093/ecco-jcc/jjaa201.
[63] Riollano-Cruz M, Akkoyun E, Briceno-Brito E, et al. Multisystem inflammatory syndrome in children related to COVID-19: a New York City experience. J Med Virol 2020. https://doi.org/10.1002/jmv.26224.