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Original Article

COVID-19-associated multisystem inflammatory syndrome in children: Experiences of three centres in Turkey

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ABSTRACT

Background: The pathogenesis and clinical manifestations of the multisystem inflammatory syndrome in children (MIS-C) has not yet been fully elucidated and there is no clear consensus on its treatment yet.

Objectives: To evaluate our patients diagnosed with MIS-C and present them to the literature in order to contribute to the better understanding of this new disease, which entered paediatric practice with the SARS-CoV-2 peak.

Methods: In this study, 17 MIS-C cases diagnosed according to the Centers for Disease Control and Prevention criteria were included.

Results: Of the patients, 7 (41.2%) had a comorbidity. Gastrointestinal system involvement was the most prominent in the patients (70.6%). Laparotomy was performed in 3 patients due to acute abdomen. Two patients had neurological involvement. Of the patients, 15 (88.2%) received intravenous immunoglobulin and 13 (76.5%) received both intravenous immunoglobulin and methylprednisolone. Two patients received invasive mechanical ventilation and 4 patients received high flow rate nasal cannula oxygen therapy. One of our patients who needed invasive mechanical ventilation and high vasoactive-inotrope support died despite all supportive treatments including plasmapheresis and extracorporeal membrane oxygenation.

Conclusions: MIS-C picture can have a fatal course and may present with severe gastrointestinal and neurological signs. Unnecessary laparotomy should be avoided.

KEYWORDS: COVID-19; gastrointestinal; Kawasaki disease; multisystem inflammatory syndrome in children; pandemic

Introduction

The heterogeneous clinical presentation of coronavirus disease 2019 (COVID-19) in children and the prominence of extrapulmonary symptoms such as gastrointestinal symptoms suggest that there are many aspects of the virus yet to be discovered [1]. Towards the end of April 2020, a clinical picture similar to COVID-19-associated incomplete Kawasaki syndrome and toxic shock syndrome was reported in children firstly in England and Italy and then in many countries [2–4]. Since this date, children with a similar clinical picture have been reported from various parts of the world, and the disorder has been defined as multisystem inflammatory syndrome in children (MIS-C) [5]. MIS-C which is thought to be caused by an abnormal immune response against severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has been identified as a rare but serious complication of COVID-19 infection in children, and its incidence rate is not fully known [6].

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It is not yet known whether MIS-C is an infectious immune reaction that occurs with the abnormal development of acquired immunity or is a new disease [7]. The disorder can lead to mortal or serious consequences. Early diagnosis and multidisciplinary management of the disease are extremely important. Although there is not yet a clear consensus on the management of MIS-C cases, treatment is usually arranged by the clinician depending on the severity of the disease. Case reports with different clinical pictures from the first case to the present day are presented in the literature [8]. Gastrointestinal involvements have been reported to be particularly prominent in these cases [9].

In this study, we present the clinical and laboratory findings and treatment approaches of our MIS-C cases who were hospitalised in three centres of two cities in our country. We aimed to contribute to the paediatric literature by sharing our own clinical experience on MIS-C, a puzzle that has not yet been fully solved.

Materials and methods

The study included MIS-C patients who were followed up in three centres (Research Hospital of Suleyman Demirel University, Malatya Training and Research Hospital and Isparta City Hospital) between November 2020 and February 2021. Two of the centres in the study were from the Isparta province in the Western Mediterranean region of Turkey and the third centre from the Malatya province in the Eastern Anatolia region. These three centres in both provinces serve a population of approximately 1.6 million. About 4,00,000 of this population is in the <19 age group.

Children <19 years of age who fulfilled the MIS-C diagnostic criteria were included in the study. The diagnosis of MIS-C was made according to the criteria described by the Centers for Disease Control and Prevention [10]. The demographic and clinical characteristics, laboratory and imaging results, applied treatment regimens, echocardiography findings, need for intensive care, invasive mechanical ventilation (IMV) or non-invasive mechanical ventilation need, and vasoactive-inotrope support need of the patients included in the study were retrospectively obtained from file records.

Vasoactive inotropic score (VIS) was calculated with the following formula: VIS = 1× dopamine [μcg/kg/min] + 1× dobutamine [μcg/kg/min] + 100× epinephrine [μcg/kg/min] + 100× norepinephrine [μcg/kg/min] + 10× milrinone [μcg/kg/min] + 10,000× vasopressin [U/kg/min].

The study was carried out by obtaining approval from the T.R. Ministry of Health and Suleyman Demirel University Ethics Committee. Written permission was obtained from the children and/or their families included in the study.

Statistical analysis

Statistical analyses of the demographic and clinical characteristics were performed using the Statistical Package for the Social Sciences 26 software. Clinical characteristics and laboratory findings were evaluated. Frequencies, percentages, and median values were used.

Table 1. Demographic and clinical characteristics of patients ($n = 17$).

Age, years, median (min–max)	10 (0.25–17)
Female sex	11 (64.7%)
Weight, kg	33* (6–80)
BMI, kg/m^2	18.2* (13.2–32)
Comorbidity	7 (41.2%)
Overweight/obesity	3 (17.6%)/1(5.9%)
Symptoms	
Fever	17 (100%)
Mucocutaneous involvement	2 (11.8%)
Conjunctivitis	6 (35.3%)
Rash	6 (35.3%)
Abdominal pain	12 (70.6%)
Acute abdomen	5 (35.7%)
Acute abdominal surgery	3 (17.6%)
Diarrhoea	7 (41.2%)
Lymphadenopathy	4 (23.5%)
Limb oedema	8 (47.1%)
Headache	4 (23.5%)
Dyspnoea	6 (35.3%)
Hypotension	5 (29.4%)
Neurologic involvement	5 (29.4%)
Kawasaki disease/atypical	3 (17.6%)/3 (17.6%)
Renal impairment	0 (0%)
Pharyngalgia	7 (41.1%)
Myalgia	6 (35.2%)
Arrhythmia	1 (5.9%)
İmpaired cardiac function	3 (17.6%)

*Minimum and maximum.

Results

There were 17 patients (third from Research Hospital of Suleyman Demirel University, six from Malatya Training and Research Hospital, and three from Isparta City Hospital) who met the diagnostic criteria. All of them developed the MIS-C clinical picture 3–4 weeks after an infection with COVID-19 during its peak in our country. Eleven (64.7%) of the cases were female. The median age of the patients was 10 years (4 months to 17 years). Their median weight was 33 kg (6–80 kg), and their median body mass index was 18.2 kg/m^2 (13.2–32 kg/m^2).

Of the patients, seven (41.2%) had a comorbid condition: three were overweight and one was obese. The other three patients had comorbidities including prematurity, aplastic anaemia, and biotinidase deficiency. Ten (58.8%) of the patients were followed up in the intensive care unit. The most common presenting complaints of the patients were fever (100%), abdominal pain (70.6%), extremity oedema (47.1%), and diarrhoea (41.2%). Of the six patients with acute abdomen, three were operated. Two of those were operated for acute apandicitis because of suggestive findings on ultrasound. However, these patients had free fluid in the abdomen, diffuse edematous appearance, and lymphadenitis. The other patient was operated with a prediagnosis of ileus, had diffuse inflammation and fibrin adhesions in the abdomen.

Of the patients, 3 (17.6%) were nasopharyngeal SARS-CoV-2 reverse transcription-polymerase chain reaction (RT-PCR) positive, 11 (64.8%) were anti-SARS-CoV-2 immune globulin G positive, and 4 (23.5%) patients were considered to be in-home contact. The demographic characteristics of the patients are presented in Table 1, clinical

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Table 2. Clinical features of patients.

Patient	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Age (years)/sex	12/F	14/M	10/M	16/F	15/M	11/F	9/M	7/F	0.5/F	7/F	1/M	10/F	11/F	0.25/F	8/M	1/F	17/F
Nasopharyngeal SARS-CoV-2 PCR	+	+	−	−	−	−	−	−	+	−	−	−	−	−	−	−	−
Anti-SARS-CoV-2 immunoglobulin G	N/A	N/A	N/A	+	+	N/A	+	+	+	N/A	N/A	+	+	+	+	+	+
Presenting symptoms																	
Fever	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Diarrhoea	+	−	−	+	+	−	−	−	+	−	+	−	+	+	−	−	−
Abdominal pain/emesis	+	−	+	+	+	−	+	+	−	+	+	+	+	+	+	−	−
Rash	−	−	−	−	−	−	−	+	−	−	+	+	+	−	+	−	+
Conjunctivitis	−	−	−	−	−	−	−	+	−	−	+	+	+	−	+	−	+
Fissured lips/strawberry tongue	−	−	−	−	−	−	−	−	−	−	−	+	+	−	−	−	−
Lymphadenopathy	−	−	−	−	−	−	+	+	−	−	+	+	−	−	−	−	−
Extremity oedema	+	−	+	−	−	−	+	+	+	−	−	+	+	−	+	−	−
Headache	−	−	−	−	−	−	+	+	−	−	−	+	+	−	−	−	−
Altered mental status/irritability	−	−	−	−	−	−	+	+	−	−	−	+	+	+	−	−	−
Respiratory failure	+	+	−	+	+	−	+	+	−	−	−	−	−	−	−	−	−
Shock	−	−	−	−	+	−	+	+	−	−	−	+	−	−	−	−	−
Echocardiography	N	N	N	N	*LVF	N	N	*MI, AI	N	N	N	*LVF, MI	N	N	*LVF, MI	N	N
PICU patient	+	+	+	+	+	−	+	+	−	−	−	+	+	+	−	−	−
Ventilation support	HFNC	IMV	−	HFNC	IMV	−	HNFC	HFNC	−	−	−	−	−	−	−	−	−
Vasoactive-inotropic support	−	−	−	−	+	−	+	+	−	−	−	+	−	−	−	−	−
VIS	−	−	−	−	60	−	15	10	−	−	−	20	−	−	−	−	−
Anti-inflammatory therapies																	
Doses of IVIG (g/kg)	2 + 1	2 + 1	2 + 1	2 + 1	2 + 1	2	2 + 1	2 + 1	2	2	2	2 + 1	2 + 1	−	2	−	2 + 1
Methylprednisolone (2 mg/kg/day, 6–8 week)	6	6	6	6	8	6	8	8	6	−	−	8	6	−	6	−	6
Methylprednisolone (30 mg/kg/day, first day)	+	+	−	+	+	−	+	+	−	−	−	+	−	−	+	−	−
Enoxaparin (1 mg/kg/dose, every 12 h)	+	+	−	+	+	−	+	+	−	−	−	+	−	−	+	−	−
Tocilizumab (4 mg/kg/day, 2 days)	−	4	−	−	4	−	−	−	−	−	−	−	−	−	−	−	−
Anakinra (5 mg/kg/day, 5 days)	−	−	−	−	+	−	−	−	−	−	−	−	−	−	−	−	−
Plasmapheresis	−	−	−	−	+	−	−	−	−	−	−	−	−	−	−	−	−
ECMO	−	−	−	−	+	−	−	−	−	−	−	−	−	−	−	−	−

*LVF: Left ventricular failure, MI: mitral insufficiency, AI: aortic insufficiency, PICU: Pediatric Intensive Care Unit, HFNC: High-flow nasal cannula, IMV: Intermittent Mandatory Ventilation.

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Table 3. Laboratory findings of patients.

Patient	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
White blood cell count ($\times 10^3/\mu l$)																	
Initial	9.19	12.17	4.02	0.2	6.13	1.6	8	14.3	22.3	19.3	12.4	7.02	4.7	15.3	11.1	5.1	12.7
Maximum	13.16	13.6	11.48	0.3	44.75	4.9	12.5	19.2	30.5	19.3	12.4	7.02	14.9	15.3	11.1	5.1	18.5
Ref 5.2–12.4 $\times 10^3/\mu l$																	
Absolute lymphocyte count (cells/μl)																	
Initial	1.12	0.56	0.37	0.1	0.49	0.52	0.4	0.3	6.7	2	2.1	0.53	0.22	3.7	0.7	0.5	9.6
Minimum	1.12	0.36	0.29	0.06	0.49	0.52	0.2	0.3	6.7	2	2.1	0.3	0.18	3.7	0.7	0.2	9.6
Ref 1.3–3.4 $\times 10^3/\mu l$																	
Haemoglobin (g/dl)																	
Initial	9.7	12.2	11.9	3.1	13.5	11.1	12.8	12.2	8.2	11.6	12.1	13.5	12.5	11.2	12.7	13.1	12.6
Minimum	8.8	10.6	8.7	3.1	10.8	9.8	9.2	10.3	8.2	10.4	10.9	11.5	11.4	10	9.9	10.7	12.4
Ref 13.6–17.2 g/dl																	
Platelets ($\times 10^3/\mu l$)																	
Initial	171	301	42	61	104	259	174	176	564	447	263	145	105	462	168	199	229
Minimum	336	350	375	43	248	431	42	70	564	650	688	408	510	956	168	183	229
Ref 156–373 $\times 10^3/\mu l$																	
Initial sodium (mmol/l)																	
Ref 136–146 mmol/l	137	134	134	132	134	132	136	131	139	136	132	132	131	137	129	137	137
Alanine aminotransferase (U/l)																	
Initial	28	103	131	97	19	10	23	54.8	9.8	131	20	38	37	27	22.9	151	37
Maximum	69	236	152	97	24	46	41	54.8	20.7	942	36	79	37	73	22.9	151	896
Ref 0–34 U/l																	
CRP (mg/l)																	
Initial	29.68	19.83	9.18	21.68	23.78	8.73	109	289	77.9	149	69.3	197	127	5.8	125	28.9	15
Maximum	29.68	24.81	13.36	32.2	24.7	16.12	209	289	77.9	149	81	197	127	67.4	125	42.8	15
Ref 0–5 mg/l																	
Procalcitonin (ng/ml)																	
Initial	21.35	0.5	0.8	1.4	3.6	0.16	4	19.1	45.8	N/A	N/A	7.04	N/A	N/A	88	0.2	N/A
Maximum	21.35	0.8	0.8	1.4	3.6	0.2	7.6	29.8	45.8	N/A	N/A	7.04	N/A	N/A	88	0.2	N/A
Ref >2 ng/ml																	
Albumin (g/dl)																	
Initial	2.2	3.2	2.7	2	2.5	3.4	3.9	3.2	2.36	3.3	4	4.3	4.5	4.1	3.1	3.2	4.1
Minimum	2.1	2.3	2.4	1.7	2.5	2.5	2.3	2	2.36	2.7	3.1	2.9	2.9	3.8	2	2.2	3.8
Ref 3.5–5.2 g/dl																	
D-dimer (ng/ml)																	
Initial	340	701	445	132	168	125	621	6476	654	1259	1757	12,800	15,130	N/A	1957	1887	14,300
Maximum	610	701	790	420	450	125	5165	6476	654	2462	2320	12,870	15,130	N/A	1957	3648	14,300
Ref 69–243 ng/ml																	
Ferritin (ng/ml)																	
Initial	1466	740	>2000	>2000	1251	538	833	592	432	316	252	4714	867	N/A	570	331	341
Maximum	1466	1632	>2000	>2000	1723	830	833	1753	432	316	252	4714	1546	N/A	570	493	341
Ref 4.6–204 ng/ml																	
Sedimentation	N/A	N/A	N/A	N/A	84	91	26	35	39	N/A	N/A	21	24	N/A	58	5	6
Ref 0–20 mm/h																	
Fibrinogen	334	883	440	550	563	495	587	568	235	681	653	N/A	N/A	NA	572	227	261
Ref 200–393 mg/dl																	
Troponin	0.019	0.023	0.013	0.003	5.5	0.003	0.035	0.025	0.006	0.003	0.003	6.4	0.003	0.020	0.024	0.003	0.003
Ref 0–0.014 ng/ml																	

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characteristics in Table 2, and laboratory values in Table 3. C-reactive protein (CRP) level is significantly higher in patients with gastrointestinal complaint (96 vs 29 mg/l, $p = .032$). Also, platelet count is significantly lower (125 vs $318 \times 103/mm^3$, $p = .002$) and lymphocytes count is lower (but not significantly, 460 vs $2910/mm^3$, $p = .051$) in acute abdomen group.

Lung computerised tomography revealed bilateral opacity in one patient, bilateral pleural effusion in three patients, bilateral opacity and bilateral pleural effusion in two patients, and ground-glass opacity in one patient. Echocardiographic examination showed left ventricular systolic dysfunction in three patients and valve insufficiency in one patient. While a patient who presented with lower extremity paralysis was diagnosed as Guillain–Barré syndrome (GBS), a reversible lesion was found in the corpus callosum splenium in the brain magnetic resonance imaging of another patient who presented with drowsiness and meaningless speech. She was diagnosed with reversible splenial lesion syndrome (RESLES). No neurological sequelae remained in these two patients, who responded dramatically to intravenous immunoglobulin (IVIG) therapy.

In the treatment, IVIG was administered to 15 (88.2%) patients. IVIG at 2 g/kg was administered to 5 (29.4%) patients once and 10 (58.8%) patients twice. Methylprednisolone was administered to 13 (76.5%) patients. Eight (47.1%) of these patients received methylprednisolone as pulse therapy. Both IVIG and methylprednisolone were administered to 13 (76.5%) patients. Two (11.8%) patients received tocilizumab, one (5.9%) patient anakinra, and one (5.9%) patient plasmapheresis. The correlation of Harada and Kobayashi score positive group with the IVIG refractory group showed no statistically significant difference (Harada $p = .74$ and Kobayashi $p = .57$).

One patient who had acute respiratory distress syndrome, myocarditis, and heart failure picture. He was followed up with IMV support received anti-inflammatory treatments including tocilizumab and anakinra upon the progression of cytokine release syndrome. His VIS was 140. Plasmapheresis was administered five times as there was no improvement in his clinical situation. However, his systolic dysfunction due to myocarditis progressed and ejection fraction decreased to 30%, and the patient died despite the extracorporeal membrane oxygenation (ECMO) treatment.

Vasoactive-inotrope treatment was administered to four (23.5%) patients. Albumin therapy was applied to eight (47.1%) patients who developed hypoalbuminaemia. Eight (47.1%) patients received anticoagulant treatment. Ten (58.8%) patients were discharged with prophylactic acetylsalicylic acid at an anti-aggregant dose.

Empirical antibiotic treatment was given to all patients for 7–10 days. Vancomycin and meropenem were given to three patients; vancomycin, meropenem, and amikacin to two patients; vancomycin, meropenem, and metronidazole to four patients with significant gastrointestinal involvement; vancomycin and ceftriaxone to five patients; and ceftriaxone to three patients. Favipiravir was additionally administered to two (11.8%) patients. Immune plasma was not administered to any patient. Two (11.8%) patients received IMV and four (23.5%) patients received oxygen with high flow rate nasal cannula. Eleven (64.7%) patients did not need oxygen therapy.

In summary, one of our patients died due to myocarditis and heart failure despite all anti-inflammatory, extracorporeal support, and mechanical support treatments. Our 16 patients who presented with different signs and symptoms were discharged with full recovery.

Discussion

In the published case series, 52–74% of the patients were previously healthy children. The most common comorbidities were reported as overweight, obesity, primary immunodeficiency, asthma, and prematurity [11–13]. Of our cases, seven had a comorbidity. Three of them were overweight, one was obese, one was born prematurely, one had aplastic anaemia, and one had biotinidase deficiency. Similar to the reported cases in the literature, being overweight/obese was a common comorbidity, and most of the children (58.8%) in our study were previously healthy.

In the literature, fever has been reported as the most common symptom at the first admission of the MIS-C cases with a rate of 82–100% [11–13]. Fever was present among the first presenting complaints in all of our cases. Previous studies have reported that 42–52% of the patients had skin rash and 26–33% had extremity oedema [11–13]. Among our cases, six (35.3%) had skin rash and eight (47.1%) had extremity oedema.

Respiratory symptoms may not be present in all cases of MIS-C. In published studies, the rate of respiratory problems has been reported to be between 9.6% and 48% [11–13]. Respiratory problems were observed in 35.3% of our cases. While two of our patients needed IMV, four were administered oxygen therapy with high flow rate nasal cannula.

In the literature, the need for vasoactive and inotropic drugs in MIS-C patients has been reported as 29.6–63% [11–13]. In four (23.5%) of our cases, inotropic support was needed. ECMO was administered to one patient with a VIS of 140 and severe myocarditis, and the course of this case was fatal. Notably, the patient was completely healthy before the disease and did not have any comorbidity.

Gastrointestinal findings may be prominent in MIS-C cases. In the literature, eight paediatric cases presenting with atypical appendicitis have been reported from the UK [14]. All of the patients in that series were admitted with fever, vomiting, abdominal pain, and diarrhoea, and radiological imaging revealed lymphadenopathy in the abdomen, fatty and inflamed mesentery, and terminal ileitis in all of these children with elevated inflammatory markers. While four of the cases needed inotropic support in the intensive care unit, ECMO was required in one case. It has been reported that all patients received broad-spectrum antibiotherapy and antiviral treatments for COVID-19, while four patients were administered IVIG and methylprednisolone treatments, with a positive response [11]. Similarly, an 8-year-old patient presented with fever and abdominal pain, whose imaging revealed multiple lymphadenopathies in the abdomen, and inflammation in the terminal ileum and caecum [15]. In the follow-up of the patient with a negative RT-PCR performed due to fever, the need for intensive care developed due to the picture of septic shock, and the patient's antibiotherapy spectrum was extended. IVIG was added to the treatment of the patient who

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was found to be positive for COVID-19 RT-PCR on the 10th day of the disease due to a deteriorating clinical course and clinical improvement was observed during the follow-up of the patient [16].

Of our cases, 12 presented with abdominal pain and 6 with clinical findings similar to acute abdomen. Abdominal imaging of these cases revealed findings such as mesenteric lymphadenitis, typhlitis, and terminal ileitis. Laparotomy was performed in three of six patients due to acute abdomen. Two patient had free fluid in the abdomen, diffuse oedematous appearance, and lymphadenitis, and the other patient who was operated with the pre-diagnosis of ileus had diffuse inflammation and fibrin adhesions in the abdomen. In the study of Amisha *et al.*, CRP values were found to be high in the appendicitis and MIS-C groups [17]. In our study, CRP level is significantly higher in patients with gastrointestinal complaint. In addition, platelet count is significantly lower and lymphocytes count is lower (but not significantly) in acute abdomen group. When we evaluate all the findings, high CRP level is associated with gastrointestinal findings. Thrombocytopenia and/or lymphopenia may indicate an acute abdomen.

In one study, the rate of elevated liver transaminases has been reported as 22% [18]. In our series, alanine aminotransferase values higher than twice the upper limit were found in 52.9% of the patients. Two patients had transaminase elevation of more than 10 times the upper limit. It was thought that this situation developed due to toxic hepatitis caused by COVID-19 or the drugs used.

Some of the children with MIS-C have been reported to develop neurological symptoms and splenial changes on brain imaging. Bektaş *et al.* have presented two cases with clinical manifestations of MIS-C who were diagnosed as RESLES [19]. Recently, there have been many paediatric case reports describing the association between COVID-19 and GBS [20, 21]. Among our patients, two had neurological manifestations. One of them presented with GBS findings, and the other developed a clinical picture consistent with RESLES diagnosis. Both of them recovered with IVIG and supportive therapy without any sequelae.

In one study, the mortality rate of MIS-C cases has been reported as 1.5% [13]. In our study, the mortality rate was 5.9%. This situation can be explained by the low number of patients and the fact that we follow up primarily severely affected cases in our centres.

Specific MIS-C treatment should be administered by a multidisciplinary team consisting of paediatric infectious diseases, cardiology, rheumatology, and intensive care specialists. IVIG treatment at the recommended dose and duration as in Kawasaki disease guidelines has been found to be successful in cases with a presentation similar to Kawasaki disease or toxic shock syndrome, particularly when myocardial dysfunction is present. Besides IVIG, methylprednisolone is the most commonly used anti-inflammatory drug. Anti-interleukin-6 monoclonal antibody (tocilizumab and sarilumab), interleukin-1 receptor antagonist (anakinra), or tumour necrosis factor-α antagonist (infliximab) have been tried in cases that are resistant to IVIG treatment and in cases with persistently raised inflammatory markers. In a series of 35 paediatric patients with COVID-19-associated MIS-C diagnosis and cardiac failure, it has been stated that most of the cases responded to IVIG treatment; 34% of the patients with atypical Kawasaki disease were additionally administered methylprednisolone, and a response was obtained with anakinra for persistent severe inflammation in three patients [22]. In 15 (88.2%) of our cases, IVIG was administered and fever was reduced dramatically after IVIG treatment. IVIG was given twice to 10 patients. Kobayashi score and Harada score were not useful in differentiating IVIG refractory cases in this series. One of the patients receiving two doses of IVIG was the child who was diagnosed with GBS. When the clinical response was not complete, repeated doses of IVIG were administered. Methylprednisolone was given in all cases except four with mild MIS-C clinical picture. The dose of methylprednisolone was adjusted according to the severity of the disease, and it was administered as pulse methylprednisolone in critically ill patients.

Similar to IVIG and corticosteroid treatments, acetylsalicylic acid at an anti-aggregant dose or low molecular weight heparin as anticoagulant therapy was administered to all patients depending on the severity of the disease. While tocilizumab was administered in two of our cases, tocilizumab and anakinra were given in addition to pulse methylprednisolone as anti-inflammatory treatment in the patient we lost, and plasmapheresis was performed five times.

The limitation of our study is that it is a retrospective study. Larger, randomised controlled prospective studies are needed to elucidate the disease spectrum, risk factors for severe disease and treatment strategies for IVIG, corticosteroids, biological modifying agents, and anticoagulation and to determine the sequelae of the disease.

Conclusions

Our study shows that COVID-19 may not only lead to involvement of the respiratory system but also to manifestations of other systems, in line with the literature. One of them is the MIS-C. Here, we want to draw attention to the fact that MIS-C may present with severe gastrointestinal system manifestations (acute abdomen) and neurological findings independent from the involvement of the respiratory system. We believe that MIS-C should be considered in paediatric patients presenting with acute abdomen during this pandemic and should be considered better before surgical intervention.

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Conflict of interest

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