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Case Series

COVID-19 related multisystem inflammatory syndrome in children: a case series from a tertiary care hospital

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ABSTRACT

Multisystem inflammatory syndrome in children (MIS-C) is a rare but serious medical condition associated with COVID-19. Approximately 40-50% of children with MIS-C meet criteria for complete or incomplete Kawasaki disease (KD). In this study, we aim to review and summarize the clinical presentation, laboratory parameters, outcome and management of MIS-C cases presenting to a tertiary care pediatric hospital of RRMCH. Here we report the case series of 7 children diagnosed with MISC. To study the clinical presentation, laboratory parameters, outcome and management of MIS-C cases presenting to a tertiary care pediatric hospital, RRMCH. Retrospective observational study done for a period of 10 months from June 2021 to March 2022. Detailed history taking, clinical examination, laboratory workup, management and outcome recorded were studied. During this period, a total of 22 children were positive for COVID-19 by RT-PCR, and 7 of these patients fulfilled the WHO criteria for MIS-C and were managed in our hospital. The study showed male preponderance with most common feature of presentation being fever constituting to 85.7%, 100% showing hyper inflammatory status and 4 out of 7 patients having cardiac involvement and zero mortality rate. Due to the increasing trend of post covid complications, strong clinical suspicion is required to diagnose MIS-C. As this condition has severe effects on major systems, awareness among pediatricians is required for timely evaluation and treatment to prevent morbidity and mortality associated with MIS-C.

Keywords: MIS-C, COVID-19, KD

INTRODUCTION

The pandemic of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has had a catastrophic effect on the human population with approximately 20% of infected persons experiencing severe or critical disease, and an overall case fatality rate of 2.3%. Although most children with COVID-19 have mild symptoms or have no symptoms at all, some children become severely ill needing hospitalization, intensive care, or ventilator support. MIS-C is a rare but serious medical condition associated with COVID-19. MIS-C is defined by inflammation in different organs such as the heart, kidneys, lungs, brain, skin, eyes, or gastrointestinal system. The causes of MIS-C remain unknown but it has been associated with SARS-CoV-2 infection. Approximately 40-50% of children with MIS-C meet criteria for complete or incomplete KD. The clinical presentation of MIS-C may also resemble that of toxic shock syndrome (TSS), secondary hemophagocytic lymphohistiocytosis, or macrophage activation syndrome (MAS).

Initially published case series from France, New-York, and England included 35, 33, and 58 children, respectively, whereas further cases are being published.[1-5] Clinical description revealed from 13 of the 30 British children aged between 4 and 14 years referred to either warm vasoplegic shock or acute abdominal and sepsis-like presentations.[10] Italian data published on May 2020

described incomplete KD-like presentations in 5 of their 10 children aged between 3-16 years of age, six of these ten patients presented with coronary inflammation and aneurysms.[4] Common observations delineated from this MIS-C referred to overlapping clinical features of KD, TSS, and macrophage activation syndrome with acute abdominal presentations upon admission.[6-10]

In this study, we aim to review and summarize the clinical presentation, laboratory parameters, outcome and management of MIS-C cases presenting to a tertiary care pediatric hospital of RRMCH

Here we report the case series of 7 children diagnosed with MISC.

CASE SERIES

Our clinical study is a case series that includes only the patients who met the world health organization (WHO) case definition of MIS-C were selected for chart review. Data were recorded in a standardized form and de identified. It is an observational, descriptive research design type of study which contains demographic information about the patients and the data was collected retrospectively. Descriptive statistics were performed and presented as mean and standard deviation (± SD) for continuous variables or as number and percentages for nominal/categorical variables. The patients were identified during the study period without a group control.

The present study was done on the clinical features and outcomes of COVID-19 serology positive patients admitted to RRMCH, Bangalore, Karnataka over a period of 10 months from June 2021 to March 2022, who met with WHO case definition of MIS-C criteria.

Since the initiation of COVID-19 screening at RRMCH (June 01 to March 20, 2022), a total of 492 COVID-19 tests were performed on individuals < 15 years old. During this period, a total of 22 children were positive for COVID-19 by RT-PCR, and 7 of these patients fulfilled the WHO criteria for MIS-C and were managed in our hospital. All patients were managed according to the diagnostic and treatment algorithms established by WHO.

The demographic data and baseline clinical characteristics are presented in Table 1. The median age was 1 year 4 months; 57.1% of patients were male. Persistent fever (85.7%) is the most common presenting symptom among the MIS-C cases in our hospital. Additionally, gastrointestinal symptoms were common among these patients presenting with vomiting (71.4%), abdominal pain (14.2%) and diarrhea (42.8%) are seen. Upper respiratory tract infection (URTI) symptoms were less prevalent in our study group, with cough experienced by one patient and conjunctivitis in 4 other patients. One of the cases were suspected to have urinary tract infection (UTI) based on initial urine microscopy, however none had urinary tract symptoms at the time of presentation or had a positive urine culture after presentation.

Laboratory test results after admission are presented in Table 2. All patients had extensive laboratory workup done upon admission or at the time when MISC was suspected. All the 7 cases in our study have been tested positive for the SARS-CoV-2 antibody. All of our MIS-C cases showed a hyper inflammatory status with remarkably high C-reactive protein (CRP), and ferritin levels, and deranged coagulation profile.

Chest radiography was performed on 6 cases, of which 2 cases showed abnormalities of bilateral perihilar infiltrates and 1 case had patchy consolidation of right upper lobe. Abdominal ultrasound (USG) was performed on 6 of 7 patients, included a variety of non-specific symptoms including increased echogenicity of liver, enlarged mesenteric lymph nodes, mild splenomegaly.

Echocardiograms were performed on all patients at diagnosis with follow up for at least 4 weeks. Cardiac involvement was seen in 4 of 7 patients. 3 patients had dilated coronaries, 1 patient had PAH and these patients received vasoactive support. Coronary-artery aneurysm was identified on the basis of a z score of 2.5 or higher in the left anterior descending (LAD) or right coronary artery (RCA). The 3 patients were placed on anticoagulation and antiplatelet therapy, of which one patient received IVIG.

Mean hospital stay of our MIS-C patients was 11 days with 5 initially requiring the PICU stay for management.

Table 1: Demographic and baseline clinical characteristics.

Variables	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Summary
Demographic data								
Age (In years and months)	3 and 3	1 and 4	3	2 and 4	3 months	1.5 months	8 months	1 and 6
Gender	F	M	M	F	M	M	F	Male, 57.1%
Clinical presentation								
Fever	Yes	Yes	Yes	Yes	Yes	No	Yes	85.7%
Rash	Yes	Yes	Yes	Yes	Yes	No	Yes	85.7%
Tachycardia	No	Yes	Yes	Yes	No	No	Yes	57.1%
Tachypnea	No	No	No	Yes	Yes	Yes	No	42.8%
Hypotension	Yes	No	No	No	No	No	No	14.2%

Continued.

Variables	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Summary
Abdominal pain	No	No	No	No	Yes	No	No	14.2%
Diarrhea	Yes	No	No	Yes	No	No	Yes	42.8%
Vomiting	Yes	No	No	Yes	Yes	Yes	Yes	71.4%
Decreased oral intake	Yes	Yes	Yes	No	No	Yes	Yes	71.4%
Cough	No	Yes	No	No	No	No	No	14.2%
Sore throat	No	No	No	No	No	No	No	0%
Conjunctivitis	Yes	Yes	Yes	Yes	No	No	No	57.1%
Seizures	No	No	No	No	No	Yes	No	14.2%

Table 2: Laboratory test results after admission.

Variables	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
RT-PCR	Negative	Negative	Negative	Negative	Negative	Negative	Negative
SARS coV2 serology	Positive	Positive	Positive	Positive	Positive	Positive	Positive
WBC (10^9/L)	27.3	27.8	17.3	3.8	14.5	7.7	16.7
Neutrophil (10^9/L)	67	50	58	51	21	32	72
Lymphocyte (10^9/L)	25	36	41	34	61	55	19
Platelets (10^3/mL)	18	700	524	88	398	32	114
CRP (mg/L)	12	12	24	12	-ve	24	-ve
Ferritin (ng/mL)	235	114.5	-	-	-	-	137
PT (sec)	16.8	15.1	18.3	14.5	17.5	15.9	12
D-dimer (mg/L)	8	80				42	
Troponin (ng/L)	0.1			0.1			
NT-proBNP (ng/L)	29881			8581			

Table 3: Hospital stay length and lab test.

Variables	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Hospital length of stay (days)	10	15	7	9	7	14	15
ICU stay (days)	6	None	None	6	3	7	8
Shock	No	No	No	No	None	Yes	None
Abnormal echocardiogram	Yes	Yes	Yes	No	Yes	No	No
LAD/RCA z-score ≥ 2.5	Yes	Yes	Yes	No	No	No	No
Abnormal CXR	No	Yes	Yes	No	No	Not done	Yes
Mechanical ventilation	None	None	None	None	None	Yes	None
Abnormal USG abdomen	Yes	Yes	Yes	No	no	Not done	Yes

Table 4: Treatment drugs given.

Variables	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
IVIG given	Yes	No	No	No	No	No	No
Corticosteroids given	Yes	Yes	yes	yes	No	No	Yes
Antibiotics	Piptaz	Ctri	Ctri	Ctri+Doxy	Piptaz+Amik	Amoxyclav+amik	Meropenem
Anticoagulants used	Yes	Yes	Yes	No	No	No	No
Ionotropic support given	No	No	No	No	No	No	Yes

DISCUSSION

The clinical profile of COVID-19 MIS-C in our study group was heterogeneous in the severity of illness, which was observed from clinically stable patients with normal or depressed myocardial function leading to circulatory shock thus requiring invasive ventilation and mechanical circulatory support. The COVID-19 virus generally binds to the ACE2 receptor, which is present on cardiac myocytes and endothelium of the vessels. Further the COVID-19 disease is known to cause a cytokine storm, especially the IL-6, 1B; IFN γ; GCSF; TNF. So based on the positive serology for covid and the elevated cytokines the COVID-19 MIS-C is predominantly an antibody mediated disease.

Here in our study, we report a case series based on the WHO MIS-C criteria guidelines. All the 7 cases showed positive SARS-CoV2 serology. In view of fever with leukocytosis and elevated inflammatory markers in

majority (5) cases, broad spectrum antibiotics were given. As there was no response in the 4 cases, corticosteroids were given for further management which helped in the final outcome and one case received IVIG. The reasons for an exaggerated inflammatory response leading to MIS-C following the SARS-CoV-2 infection are not clear, although cytokine-mediated storm has been described with other viral infections. Although initially thought to be SARS-CoV-2-associated KD, emerging data have shown MIS-C to be a separate entity with age as a distinguishing feature, supported by the median age group in our study of 1 year 4 months. Thus, illness with COVID-19 in children is infrequent but have been reported with much younger age and comorbidities being risk factors for severe disease.

As already documented in previous studies, many children with MIS-C present some criteria for complete or incomplete KD, appendicitis-like abdominal symptoms and important hyper inflammatory syndrome.[1-3,10-12] In our study many children presented with acute viral like prodrome with fever, rash, vomiting, decreased oral intake and conjunctivitis. MIS-C also differs from acute COVID-19 illness which tends to be most severe in infants <1 year of age.[4,13,14] Which is similar to our study where infants less than 1 year of age required ionotropic support and mechanical ventilation. Four out of seven cases (case 1) were given corticosteroids, one patient (case 1) was given IVIG, anticoagulants were required for 3 patients (case 1-3), ionotropic support was required for one patient (case-7). Antibiotics were required for all the seven patients in our study.

CONCLUSION

Due to the increasing trend of post covid complications, strong clinical suspicion is required to diagnose MIS-C. As this condition has severe effects on major systems, awareness among pediatricians is required for timely evaluation and treatment to prevent morbidity and mortality associated with MIS-C. Further larger multicenter studies are required to elaborate the spectrum of disease, risk factors for more severe illness, and response to supportive and medical therapies including IVIG, corticosteroids, and anticoagulation strategies. Long-term follow up will be required to determine any sequelae of MIS-C on myocardial function.

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