

Case Series

COVID-19 related multisystem inflammatory syndrome in children: a case series from a tertiary care centre in Western Uttar Pradesh

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ABSTRACT

A minority of children infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) present with multisystem inflammatory syndrome in children (MIS-C), usually 2 to 4 weeks post-infection, the pathophysiology of which is still unclear. MIS-C referred to overlapping clinical features of KD, TSS, and macrophage activation syndrome with acute abdominal presentations upon admission. This is a case series of 5 children which includes COVID-19 serology positive patients admitted to Sarojini Naidu medical college, Agra, Uttar Pradesh from May 2020 to January 2022, who met the world health organization (WHO) case definition of MIS-C. The most common presenting symptoms of MIS-C patients at our hospital were fever (100%), reduced oral intake (100%), conjunctival hyperemia (100%), rash (100%), abdominal pain (80%), diarrhea (60%) and vomiting (40%). All MIS-C patients displayed hyper inflammation, abnormal coagulation profiles, and elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and ferritin levels. High B-type natriuretic peptide (proBNP) and troponin levels were detected in 100% and 80% of the patients respectively. Two patients had ejection fractions (EF) <55% on echocardiography, indicating systolic ventricular dysfunction (case 4 and 5) with Mitral regurgitation was found in case 4 only. Broad-spectrum antibiotics, intravenous (IV) steroids and aspirin were administered to the all patients as per the ministry of health and family welfare guidelines for 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: COVID-19, MIS-C, Clinical profile

INTRODUCTION

A minority of children infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) present with MIS-C, usually 2 to 4 weeks post-infection, the pathophysiology of which is still unclear.¹ This potentially life-threatening complication of COVID-19 infection may occur during or after recovery in symptomatic as well as asymptomatic children. Spectrum of MIS-C may range from mild disease to severe involvement including shock, multiorgan dysfunction, coagulopathy, respiratory failure, myocardial dysfunction, and encephalopathy.² MIS-C referred to overlapping clinical features of KD, TSS, and

macrophage activation syndrome with acute abdominal presentations upon admission.^{3,4} 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 Sarojini Naidu medical college, Agra. Here we report the case series of 5 children diagnosed with MIS-C.

CASE SERIES

This is a case series of 5 children which includes COVID-19 serology positive patients admitted to Sarojini Naidu medical college, Agra, Uttar Pradesh from May 2020 to January 2022, who met the WHO case definition

of MIS-C. Data was recorded in a standardized form and de identified. All patients were managed according to the diagnostic and treatment algorithm established by WHO.

We assessed five cases of MIS-C, all of which were treated at our hospital and met the WHO guidelines. Three patients were male, two were female with the mean age of 4.5 years at diagnosis. All patients had previously been in good health (100%). Four patients were first admitted to the pediatric intensive care unit (PICU). The most common presenting symptoms of MIS-C patients at our hospital were fever (100%), reduced oral intake (100%), conjunctival hyperemia (100%), rash (100%), abdominal pain (80%), diarrhea (60%) and, vomiting (40%). None of the case presented with upper respiratory tract infection (URI) symptoms (Table 1).

All patients showed high Ig G COVID antibody titers. All patients underwent comprehensive laboratory testing upon admission or when MIS-C was suspected. Three patients were lymphopenic for their age, and all patients had high total white blood cell (WBC) counts ($>13 \times 10^3/l$; 100%). All MIS-C patients displayed hyperinflammation, abnormal coagulation profiles, and elevated CRP, ESR, and ferritin levels. High B-type natriuretic peptide (proBNP) and troponin levels were detected in 100% and 80% of the patients respectively. Four patients had thrombocytopenia and one had thrombocytosis. Both blood and urine cultures were

negative in all cases. Antigen and serology tests for malaria, typhoid, dengue and leptospirosis were also negative in all cases (Table 2 and 3).

The most frequent abnormality found on chest radiography was bilateral mild pleural effusion which was seen in two cases case 4 and 5 (50%). Two patients who underwent abdominal ultrasonography followed by abdominal computed tomography (CT), which revealed multiple sub-centimetric mesenteric lymph nodes with mild ascites in case 3 and 4. In case 2 ultrasonography revealed mild hepatomegaly associated with elevated liver function enzymes, which subsided after two weeks of follow-up. All patients underwent echocardiography at the time of diagnosis. Echo was repeated on follow-up in all patients at four weeks and patients with abnormal results underwent echocardiography at 8 weeks or earlier. Two patients had EF $<55\%$, indicating systolic ventricular dysfunction (case 4 and 5) with Mitral regurgitation was found in case 4 only. Case 4 had required inotropic support to maintain blood pressure not responding to fluids. The average length of hospital stay for the MIS-C patients in this study was 11 days. Broad-spectrum antibiotics, IV steroids and aspirin were administered to all patients as per the ministry of health and family welfare guidelines for MIS-C. All patients received aspirin throughout their hospital stay and at discharge to prevent coronary thrombosis. All our patients achieved full recovery and left hospital in good health (Table 4).

Table 1: Patients characteristics and clinical presentation of the patients diagnosed with paediatric multi system inflammatory syndrome.

Variables	Case 1	Case 2	Case 3	Case 4	Case 5	Summary
Age (in years)	4	3.5	3	4	8	4.5 (Mean)
Sex	Female	Male	Female	Male	Male	Male, 60%
Chronic diseases	No	No	No	No	No	Healthy, 100%
Fever	Yes	Yes	Yes	Yes	Yes	100%
Abdominal pain	No	Yes	Yes	Yes	Yes	80%
Conjunctival hyperemia	Yes	Yes	Yes	Yes	Yes	100%
Rash	Yes	Yes	Yes	Yes	Yes	100%
Diarrhea	Yes	No	No	Yes	Yes	60%
Vomiting	No	No	Yes	Yes	No	40%
Hypotension	No	No	No	Yes	No	20%
Decreased oral intake	Yes	Yes	Yes	Yes	Yes	100%

Table 2: Laboratory results of the patients diagnosed with paediatric multi system inflammatory syndrome.

Variables	Case 1	Case 2	Case 3	Case 4	Case 5	Summary
Platelet count (1.5-4.5 lac/mm ³)	1.4	1.2	4.2	0.31	1.5	Thrombocytopenia in 80% cases, thrombocytosis in 20%
INR (0.80-1.10)	1.2	1.3	1.1	2.2	1.6	80% above normal range
PT (9.70-14.10)	15.5	16.2	14.1	18.4	20.4	80% above normal range
APTT (24.7-31.5)	35.5	34.6	31.5	40.4	34.8	80% above normal range
Hb (11-14 g/dl)	9.5	9.8	10.1	8.5	10.7	Anemia in 100% cases range
TLC (5000-13000 cells/mm ³)	26100	13300	21000	18000	13700	100% above normal range
Neutrophil (45-65%)	95	82	84	74	85	100% above normal range
Lymphocyte (35-45%)	3	15	12	20	12	100% below normal range

Continued.

Variables	Case 1	Case 2	Case 3	Case 4	Case 5	Summary
SGOT (5-40 IU/l)	22.65	130.4	22.87	21.16	16.24	20% above normal range
SGPT (5-42 IU/l)	23.16	120.8	28.01	26.33	10.81	20% above normal range
SARS-COV-2 igM and igG serology tests	igG+, igM -	igG+, igM -	igG+, igM -	igG+, igM -	igG+, igM -	100% positive
SARS-COV-2 RT-PCR test	-ve	-ve	-ve	-ve	-ve	100% negative

Table 3: Laboratory results of the patients diagnosed with paediatric multi system inflammatory syndrome.

Variables	Case 1	Case 2	Case 3	Case 4	Case 5	Summary
D-dimer (<0.50 mg/l)	>10	>10	>10	>10	>10	100% above normal range
Ferritin (70-140 ng/ml)	1240.8	1580.6	1250.4	1315.1	1100.1	100% above normal range
Troponin (<73 ng/ml)	5	113.5	2.3	427.8	152.3	60% above normal range
PRO BNP (<300 pg/ml)	1446.0	5015.0	1670.0	1560.0	3566.0	100% above normal range
Albumin (2-3.5 g/dl)	2.1	2.7	2.5	1.9	1.5	40% below normal range
Creatinine (0.31-1.20 mg/dl)	0.66	0.61	0.91	0.61	0.51	100% normal range
Urea (13-43 mg/dl)	26.35	26.06	23.51	28.12	29.61	100% normal range
ESR (13-18 mm/1 h)	42	45	44	43	45	100% above normal range
CRP (<5 mg/l)	67.48	72.48	61.51	191.8	32.11	100% above normal range
LDH (<350 U/l)	814.2	1254.3	974.6	1500.3	870.2	100% above normal range

Table 4: Clinical outcome and treatment of the patients diagnosed with paediatric multi system inflammatory syndrome.

Clinical outcome	Case 1	Case 2	Case 3	Case 4	Case 5	Summary
Hospital length of stay (days)	15	10	6	15	9	11 (mean)
ICU stay (days)	5	4	0	7	3	3.8 (mean)
Mechanical ventilation	No	No	No	No	No	Not required
Shock	No	No	No	Yes	No	20% abnormal
Abnormal echocardiogram	No	No	No	Yes	Yes	40% abnormal
Abnormal CXR	No	No	No	Yes	Yes	40% abnormal
Abnormal US abdomen	Normal	Abnormal	Abnormal	Abnormal	Normal	60% abnormal
IVIg	No	No	No	Yes	No	20% required
Corticosteroids	Yes	Yes	Yes	Yes	Yes	100% required
Antibiotics	Yes	Yes	Yes	Yes	Yes	100% required
Inotropes	No	No	No	Yes	No	20% required
Aspirin	Yes	Yes	Yes	Yes	Yes	100% required
Outcome	Discharge	Discharge	Discharge	Discharge	Discharge	100%

DISCUSSION

We report case series of 5 cases which are diagnosed based on WHO MIS-C criteria guidelines. In our study out of five cases three patients were male, two were female with the mean age of 4.5 years at diagnosis which is similar to study by Maheshwari et al.⁵ The most common presenting symptoms of MIS-C patients at our hospital were fever (100%), reduced oral intake (100%), conjunctival hyperemia (100%), rash (100%), abdominal pain (80%), diarrhea (60%) and vomiting (40%). Similar to our findings review of 1415 patients from 31 studies across the globe reported predominance of gastrointestinal symptoms and a lesser frequency of patients experiencing respiratory symptoms.⁶ Three patients were lymphopenic for their age, and all patients had high total white blood cell (WBC) counts ($>13 \times 10^3/l$; 100%) which is similar to study done by

Dhanalakshmi et al and Shobhavat et al.^{7,8} Four patients had thrombocytopenia and one had thrombocytosis, similar to our study thrombocytopenia was found in Balagurunathan et al, Shobhavat et al in 40% and 71% cases respectively.^{8,9}

All MIS-C patients displayed hyperinflammation, abnormal coagulation profiles, and elevated CRP, ESR, and ferritin levels, which is comparable to studies done by Angurana et al.¹⁰ Balagurunathan et al biomarkers of cardiac dysfunction, troponin and pro-Brain natriuretic peptide (pro-BNP) were also reported to be deranged in Balagurunathan et al, Angurana et al, similar to our study.^{9,10} Two patients had EF<55%, indicating systolic ventricular dysfunction (case 4 and 5) comparable to study done by Jain et al where left ventricular systolic dysfunction (41%) and coronary dilation (28%) were the most common findings on echocardiography.¹¹ The most

frequent abnormality found on chest radiography was bilateral mild pleural effusion which was seen in two cases case 4 and 5. Broad-spectrum antibiotics, IV steroids and aspirin were administered to the majority of patients as per the ministry of health and family welfare guidelines for MIS-C. All our patients achieved full recovery and left the hospital in good health.

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. The gastrointestinal system was the most commonly affected system in MIS-C followed by the hepatic and cardiovascular systems. Cases responded well to IVIg and steroids. Overall, the short-term prognosis was good in our study population. We recommend further studies monitoring the long term effects of MIS-C through follow-up evaluations. Many such studies are ongoing and results awaited.

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