Pediatric Oncall Journal (Jul-Sep 2021)
Volume 18, Issue 3: 87-89
DOI: https://doi.org/10.7199/ped.oncall.2021.29

PEDIATRIC ONCALL
CHILD HEALTH CARE

CASE REPORTS

DON'T MISS THE MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN (MIS-C): A YOUNG INFANT PRESENTING AS CARDIOGENIC SHOCK

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ABSTRACT
A 45-days old infant presented with features of multisystem inflammatory syndrome in children (MIS-C) along with positive SARS-CoV-2 antibody and negative PCR/antigen test. Clinical presentations were fever, respiratory distress with cardiogenic shock. The child required ventilator support, vasoactive drug and immunomodulation to which he responded. We present this case as MIS-C has rarely been reported in this age group.

ARTICLE HISTORY
Received 9 June 2021
Accepted 19 June 2021

KEYWORDS
Multisystem inflammatory syndrome, Cardiogenic shock, Immunomodulation, Temporal association.

Introduction

A novel coronavirus (SARS-CoV-2) was identified in late 2019 that rapidly reached pandemic proportions. World Health Organization (WHO) designated the disease COVID-19, which stands for coronavirus disease 2019.[1] In April of 2020, reports from the United Kingdom documented a presentation in children similar to incomplete Kawasaki disease (KD) or toxic shock syndrome.[2] Since then, there have been reports of similarly affected children in other parts of the world. The condition has been termed multisystem inflammatory syndrome in children (MIS-C) temporally associated with SARS-CoV-2. The spectrum of MIS-C is characterized by an unopposed inflammatory state that may rapidly progress to multiorgan failure.[3]

Children with MIS-C present with persistent fever (100%), conjunctivitis (68%), rash (75%), elevated inflammatory markers (100%), coagulopathy (100%), gastrointestinal complaints (85%) and cardiac abnormalities (75%).[4] Three variations of the disease patterns were reported: a group of children with persistent fever and significant increase in evidence of inflammatory activity, without criteria for Kawasaki disease, shock or organ failure, a second group with Kawasaki disease criteria, and a third group with severe cardiac dysfunction, shock, coronary aneurysms, among other manifestations, including fever and gastrointestinal symptoms.[5] The presence of positive SARS-CoV-2 antigen by PCR, serological testing for antibodies or report of close contact with a person diagnosed with COVID-19 helps differentiate MIS-C from other illnesses.[5]

In this case report, we describe a 45-days old infant presenting with severe MIS-C. Patient presented with respiratory distress secondary to cardiogenic shock & qualifying criteria of MIS-C.

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Case Report

A 45-days old male child presented with fever and breathing difficulty for 3 days for which he was hospitalized in another hospital. He had received DPT vaccine 6 days ago. Both grandparents were detected to have COVID-19 infection 2 weeks prior to child's hospitalization. Child was being treated with high flow oxygen device (HFOD) and steroids for 3 days before referral to us in view of respiratory distress and worsening of clinical condition. On presentation, he had grunting, tachypnea, chest retractions, and 80% oxygen saturation (SpO2) on room air. Systolic blood pressure was 60 mm of Hg, heart rate was 160/min and capillary refill time was >6 secs. There was hepatomegaly on per abdomen examination, bilateral crepts on respiratory system examination with mottled skin and pallor. Child's weight recorded was 4.7 kg with a length of 58 cm. COVID-19 IgG was positive and COVID-19 antigen and PCR test were negative. Blood gas showed severe metabolic acidosis (pH 7.08, bicarbonate 10 mEq/L, anion gap 22, lactate 12.94 mmol/L) with central venous oxygen saturation (SCVO2) of <60%. Other investigations are depicted in table 1. Electrocardiogram (ECG) showed inverted T wave. Functional echocardiography showed distended inferior vena cava (IVC), ejection fraction (EF) 20% with dilated left ventricle suggestive of cardiogenic shock.

Patient was started on oxygen by non-rebreathing mask (NRM) ventilation. In view of shock, patient was given fluid bolus [2 aliquot of 5 ml/kg of normal saline (NS)], reassessed and started on intravenous (IV) adrenaline infusion (initially 0.5 mcg/kg/min and slowly titrated to 0.3 mcg/kg/min), with IV furosemide infusion (initially at 0.3 mg/kg/day and slowly titrated to 0.1 mg/kg/day), He was subsequently put on pressure-regulated volume control (PRVC) ventilation. IV calcium (20 mg/kg diluted with 5% dextrose) was given slowly with

Table 1. Investigations at the time of admission

Investigations	Patient's values
Hemoglobin (gm/dl)	7.4
White blood cells (cells/cumm)	21790
Neutrophils (%)	35.6
Lymphocytes (%)	62.2
Platelet count (cells/cumm)	456,000
Sodium (mmol/L)	131
Potassium (mmol/L)	5.7
Ionic calcium (gm/dl)	0.53
C-Reactive Protein (CRP) (mg/dl)	0.5
S. Creatinine (mg/dl)	0.5
SGPT (IU/L)	40
SGOT (IU/L)	86
Blood Culture	No growth
Procalcitonin (PCT) (Normal: <0.5 mcg/L)	2.42
LDH (Normal: 140-280 U/L)	2360
Interleukin 6 (IL-6) (Normal: 0-4.4 pg/ml)	35.1
NT-pro BNP (Normal: 0-300 pg/ml)	>30000
D-Dimer (Normal: 0-0.50 mcg/ml)	1.33
S. Ferritin (Normal: 50-200 ng/ml)	31400

Note: SGPT - Serum glutamic pyruvic transaminase, SGOT - Serum glutamic oxaloacetic transaminase, LDH - lactate dehydrogenase, NT-pro BNP - N-terminal pro b-type natriuretic peptide.

strict cardiac monitoring. IV antibiotics (ceftriaxone and linezolid) and other supportive measures were given. Child was diagnosed to have MIS-C and treated with 2 g/kg of IV immunoglobulin (IVIg) over 48 hours and high dose intravenous methylprednisolone (30 mg/kg/day for 3 days then 2 mg/kg/day and titrated to 1 mg/kg/day to complete 7 days) followed by oral prednisolone (1 mg/kg/day and titrated to 0.5 mg/kg/day for another 7 days) to complete total 2 weeks course along with low molecular weight heparin (LMWH) injection [1 mg/kg/day subcutaneous (SC) every 12 hourly] for total 7 days. Gradually there was resolution of cardiogenic shock along with fall in interleukin 6 (IL) level to 3.1 pg/ml) with improvement in EF (45% within 5 days). Patient was started on low dose aspirin (5 mg/kg/day) after 7 days of completion of LMWH. He was weaned off from invasive ventilation after 7 days to non-invasive ventilation (HFNC) which was successfully weaned off and stopped in next 3 days. He was discharged from the hospital after 16 days of treatment. On follow up after one month, patient was afebrile, accepting feeds with no respiratory distress and had normal cardiac evaluation.

Discussion

MIS-C associated with SARS-CoV-2 is thought to occur secondary to a cytokine storm that damages numerous organ systems.[6] The inflammatory response results in blood vessel dilation, leading to hypotension, fluid accumulation and shock.[6] Our child presented with fever followed by rapid deterioration due to cardiogenic shock and respiratory failure. It is hereby important for pediatricians to be aware of the diagnosis of MIS-C so that targeted immunotherapy can be initiated quickly.

The Centers for Disease Control and Prevention (CDC)'s case definition for MIS-C is (1) an individual less than 21 years of age presenting with fever; (2) laboratory evidence of inflammation by one or more markers (such as CRP, ESR, fibrinogen); (3) evidence of clinically severe illness requiring hospitalization, with greater than 2 organ systems involved (cardiac, renal, respiratory, hematologic, GI, mucocutaneous, or neurological); (4) no other plausible alternative diagnosis and; (5) SARS- CoV-2 infection confirmed by RT-PCR, serology, or antigen testing (or, absent a positive SARS-CoV-2 test, exposure to a suspected or confirmed COVID-19 case within 4 weeks prior to symptom onset).[7] Our patient met these criteria, hence was diagnosed as MIS-C. As we move into post-peak phase of COVID-19 illness, MIS-C is thought to be related to a post-viral immune-mediated inflammatory process.[8]

In view of the current pandemic scenario, with new data on the behavior of SARS-CoV-2, the pediatric population has gained prominence, despite the lower number of cases in relation to the adult population. Most cases of pediatric (MIS-C) temporarily associated with SARS-CoV-2 have so far seen non-fatal outcomes.[9] With a greater number of cardiac involvement than classical Kawasaki disease, presenting with myocarditis and cardiogenic shock there is a greater need for care in the Intensive Care Unit (ICU) and early diagnosis. Clinical suspicion can be difficult due to the various spectra of the disease. Early treatment, given the greater cardiac involvement in MIS-C has become the main pillar in an attempt not to increase the number of acquired heart diseases. Despite the greater number of resistant cases, the majority of MIS-C cases responded well to classic IVIG and aspirin therapy.[9]

The prognosis of MIS-C is uncertain, given that it is a relatively new clinical entity and long-term follow-up studies are lacking. The disease course in MIS-C can be quite severe, with many children requiring intensive care interventions. Most children survive, but deaths have been reported. In a systematic review of 16 case series including a total of 655 patients with MIS-C, there were 11 deaths (1.7%).[10]

Conclusion

With increase in the incidence of pediatric MIS-C, temporarily associated with SARS- CoV-2, pediatricians need to be aware of this condition. The diagnosis is challenging due to the variety of clinical and laboratory manifestations, with both positive and negative COVID-19 test results, but that should not delay therapy as soon as the diagnostic suspicion is generated. Follow-up is important, as these complications may appear later. We await further studies, given the novelty of the disease to improve the diagnosis and care of the pediatric population. To date this infant is the youngest case of severe MISC in India.

Compliance with Ethical Standards

Funding: None
Conflict of Interest: None

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