Multisystem inflammatory syndrome in children; a rare case found in Covid-19 pandemic

Mukesh Kumar Jain[1], Jyoti Ranjan Behera[1], Bandya Sahoo[2], Reshmi Mishra[3], Sagar Parida[4], *Sibabratta Patnaik[3]

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Introduction

In April 2020, a group of children with hyper-inflammatory shock were reported in England. Now many cases have been reported from across the world. We here report a case of Multisystem Inflammatory Syndrome in Children (MIS-C) detected in the Odisha state of India.

Case report

A girl aged 10 years presented with high fever with loose motions for 2 days and repeated episodes of seizures for the last 6 hours. In emergency, she was found to be obtunded with a Glasgow Coma Scale (GCS) of 6, an oxygen saturation of 87% in room air, a heart rate 128/min, a respiratory rate 26/min and blood pressure of 82/42 mm Hg. She was managed as a case of septic shock, with oxygen by non-rebreathing mask, normal saline bolus and adrenalin infusion at a dose of 1 mcg/kg/min. She was intubated and ventilated. She was managed with parenteral meropenem, vancomycin, acyclovir and levetiracetam. Investigations revealed a haemoglobin (Hb) level of 9.3g/dl and a total leucocyte count (TLC) of 20,300/cu mm (neutrophil 70% and lymphocyte 28%). Kidney function was normal. C-reactive protein (CRP) was 79.7mg/L, serum ferritin 119ng/mL, serum lactate dehydrogenase (LDH) 606.2 U/L and creatine kinase myocardial band (CK-MB) was 52 IU/L.

Reverse transcription polymerase chain reaction (RT-PCR) for Covid19 was sent. 2D-ECHO revealed decreased contractility of heart and x-ray of chest showed cardiomegaly with a cardio-thoracic ratio of 0.6. She continued to have fever with spikes despite all treatment. Her repeat tests after 3 days revealed a Hb level of 7.2 g/dL, TLC of 8800/cu mm (N 78%), total platelet count 140,000/cu mm, CRP of 210 mg/L, procalcitonin of 95.4ng/mL, LDH of 1963 U/L, d-Dimer of 3.98 mcg/mL, serum ferritin of 91.4ng/mL, erythrocyte sedimentation rate (ESR) of 26mm in 1st hour and triglyceride level of 188 mg/dL. Later RT-PCR for Covid-19 came out to be positive while antibody to Covid-19 was negative. Evaluation for fever in the form of malaria parasite immune-chromatography test (MP ICT), scrub typhus IgM, dengue IgM, blood culture, ultrasonography (USG) of abdomen, and urine examination did not reveal any abnormalities. Magnetic resonance imaging (MRI) of brain revealed cerebral oedema. After reviewing all reports, diagnosis of MIS-C was made as per criteria laid down by WHO. She was managed with intravenous immunoglobulin (IVIG) 2 g/kg over 24 hours, along with methyl prednisolone 2 mg/kg/ day in 2 divided doses for 7 days. She was weaned off inotropes in 4 days and extubated on day 7. She was re-intubated on day 9 because of low GCS. She continued to remain on the ventilator because of low GCS, her ventilator requirement gradually increasing and she finally expired on day 19 of admission.

Discussion

Different organisations give different definition for MIS-C. The definitions by Centres for Disease Control and Prevention (CDC), World Health Organisation (WHO) and the Royal College of Paediatrics and Child Health (RCPCH) are given in a tabular form (Table 1) for better understanding[2]. Our child had fever for 2 days, along with loose motions and developed seizures later. She was in shock with myocardial dysfunction with raised CPK-MB. Inflammatory markers were elevated. RTPCR for Covid-19 was positive and all possible causes of infection were ruled out. Thus she fit into the diagnosis of MIS-C. The exact pathophysiology of MIS-C is not known, but there are many hypotheses. The cytokine storm leading to multi-organ dysfunction and raised inflammatory markers may be due to antibody mediated immune enhancement just like dengue fever[3]. Direct anti-

[1]*Assistant Professor,* [2]*Professor,* [3]*Associate Professor, Department of Pediatrics,* [4]*Fellow, Pediatric Intensive Care, Kalinga Institute of Medical Sciences, Bhubaneswar, India*
**Correspondence:* drsbpatnaik45@gmail.com

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tissue antibody and immune complex mediated tissue injury and delayed cytokine surge are the other proposed hypotheses [4,5].

Table 1: ***Definitions for Multisystem Inflammatory Syndrome in Children***

	WHO (MIS-C)	CDC (MIS-C)	RCPCH (PIM-TS)
Age	0–19 years	<21 years	Child (age not specified)
Main features	Two of the following: (A) Rash or bilateral non-purulent conjunctivitis or mucocutaneous inflammation signs (oral, hands, or feet); (B) Hypotension or shock; (C) Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including echocardiogram findings or elevated troponin or N-terminal pro B-type natriuretic peptide); (D) Evidence of coagulopathy (elevated prothrombin time, partial thromboplastin time, and elevated D-dimers); and (E) acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain	Clinically severe illness requiring hospitalisation; and multisystem (two or more) organ involvement (cardiac, renal, respiratory, haematological, GI, skin, or neurological)	Single or multiple organ dysfunction Shock or respiratory, renal, gastrointestinal, or neurological disorder; additional features
Inflammation	Fever and elevated inflammatory markers for 3 days or more	Fever >24 hours and elevated inflammatory markers	Fever and elevated inflammatory markers
Exclusion	Other microbial cause of inflammation	Other plausible alternative diagnoses	Any other microbial cause
SARS-CoV-2 status	Positive RT-PCR, antigen test, or serology; or any contact with patients with COVID-19	Positive RT-PCR, serology, or antigen test; or COVID-19 exposure within the past 4 weeks before symptom onset	RT-PCR positive or negative

In the study published in the Morbidity and Mortality Weekly Report (MMWR) on August 7, 2020, almost all (99%) had evidence of SARS Cov2 infection (46% were serology positive, 25% only RTPCR positive and 27% both serology and RTPCR positive), while in 1% no test was done but epidemiologic link was present. They were broadly divided into 3 groups. First group (35%) presented with multi-organ dysfunction, shock, myocarditis, where 98% were serology positive with or without RTPCR being positive. The second group (30%) presented as pneumonia and ARDS and were mostly RTPCR positive (86%). The last group (35%) usually behaved as Kawasaki disease with maximum coronary affection. Majority in this group were antibody positive (63%) while 34% had both positive[6]. In the paper published from UK, out of total 78 cases, 76% required IVIG, 73% required steroids, while 22% needed biologic immune modulators. Forty one percent needed prophylactic anticoagulants and 58% required aspirin[7].

Our child was treated with IVIG, steroids, low molecular weight heparin and other supportive treatment. She did improve and was even extubated after the 7th day. However, because of the low GCS she was re-intubated. The death might be due to consequences of prolonged ventilation and airway related issues.

MIS-C is a rare and new clinical condition seen in children during this Covid-19 pandemic. In any child presenting with fever, multiorgan dysfunction and very high inflammatory markers, MIS-C should be thought of and the child evaluated accordingly.

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