

Multi-System Inflammatory Syndrome in Children (MIS-C) Associated With Sars-Cov-2 at a Tertiary Care Hospital – A Case Report

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I. Introduction :

SARS-CoV2 infection, since its outbreak in Wuhan of Hubei Province, China in December 2019¹ has been declared by the World health Organization (WHO) as a public health emergency of International concern and declared a pandemic on March 11, 2020.² Although children and adolescents have less severe presentations as compared to children, they are at a risk of developing secondary conditions. Multi-system inflammatory syndrome in children (MIS-C) is an emerging syndrome which was first reported in April 2020 by paediatricians in the United Kingdom.³ It is usually seen within 2-6 weeks after SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2/COVID-19) infection or positive history of COVID-19 exposure.⁴ There are various symptoms & signs described which include fever, abdominal pain, vomiting or diarrhoea, erythematous skin rash, hypotension, mucocutaneous involvement and conjunctival changes.⁵⁻⁷ Neurologic and respiratory symptoms may also occur^(5,7). However, most importantly, they can present with cardiac involvement resulting in cardiac dysfunction, shock, myocarditis and coronary artery dilatation or aneurysm⁽⁵⁻⁹⁾. There is considerable clinical overlap between MIS-C, Kawasaki's disease (KD) and SARS-CoV-2, which can be taxing from diagnosis point of view. Due to limited evidence, treatment is based on consensus guidelines. Presently, treatment is primarily with immunomodulators, aspirin and supportive care.⁹

CASE

A 12 year old male child with no significant past medical illness presented to Pediatric Emergency of the Regional Institute of Medical Sciences, Imphal, Manipur, India, a tertiary care hospital with complaints of high grade, non remitting fever alongwith progressively increasing dull aching, generalised, diffuse pain abdomen of 7 days duration; he also had moderate intensity intermittent headache of similar duration and redness of both eyes for 2 days. Though there were no other significant history, he had been tested positive for SARS-CoV-2 RT-PCR, 4 weeks previously.

On examination, the child was conscious, of average build, but febrile (102.4°F); pulse rate – 130 beats per minute; SpO₂ – 97% at room air; congestion of bilateral conjunctiva(non-purulent) and posterior pharyngeal were present; blood pressure - 90/64 mmHg (<50th centile).; there was tachypnea (respiratory rate - 44 per minute) along with chest retractions, but percussion and auscultation findings were normal. Abdomen examination revealed hepatomegaly – liver palpable 4 cm (liver span 14 cm), soft in consistency, rounded border, mild tenderness and soft splenomegaly of 2 cm; cardiovascular and central nervous system examination revealed no abnormal findings.

Laboratory findings at admission showed : mild anaemia - Hb-9.1 g/dl; total leucocyte count - 12,500/mm³; differential leucocyte count -N₉₀,L₅,M₃,E₂; ESR – 100mm1st hr; hyponatremia (128 mEq/L), hypoalbuminemia (2.5mg/dl); CRP (73.4mg/L), elevated D-Dimer (4364ng/ml) and serum ferritin (>1200ng/ml); coagulation profile and C-TROP-I were within normal limits. RT-PCR for SARS CoV-2 – negative, however antibody testing for SARS-CoV-2 (SARS-CoV-2 IgG) was positive. Blood and urine cultures were sterile. Tests for dengue, scrub typhus and typhoid were also negative. Chest X ray showed diffuse patchy opacities in the bilateral lung fields.



Fig. 1: Chest X-ray showing diffuse patchy opacities in the bilateral lung fields.

2 D ECHO showed – dilated LA 30mm (Z+ 2.52), LV(57mm (Z+3.95) and dilated coronaries; LMCA – 3.6(Z+2.09), LAD-2.3(Z+0.54), proximal RCA – 2.2mm(Z+0.35) with an EF – 57% .



Fig.2 (i)



Fig.2 (ii)



Fig.2 (iii)

Fig.2 (i – iii) : 2D ECHO showing dilated LA[2(i)], LV[2(ii)] & left main coronary artery [2(iii)]
[LA – left atrium; LV – left ventricle; LMCA ; left main coronary artery; LAD – left anterior descending; RCA – right coronary artery; EF – ejection fraction]

Child was treated with, intravenous methylprednisolone (2mg/kg/day), intravenous immunoglobulin (2gm/kg given over 24 hours), parenteral antibiotics (Inj. Ceftriaxone – 100mg/day), aspirin (3mg/kg/day) and required inotropic support [Inj. Epinephrine 0.1mcg/kg/min in the initial 4 days after pediatric intensive care unit (PICU) admission].

He recovered well (after 8 days – CRP, ESR and serum Ferritin had reduced to 32.0 mg/L, 60 mm1st hr and 766 ng/ml respectively) and was discharged with Tab. Aspirin and Prednisolone in tapering doses after 10 days of treatment. Post discharge ECHO at two weeks and 2 months were normal and he is being followed up for long term complications.

II. Discussion

Temporal association between infection with SARS-CoV-2 infection & MIS-C as a rare complication was first noted in April, 2020.³ Since then, MIS-C have been reported to occur 2-6 weeks after SARS-COV-2 infection.⁴ This is the first reported case from a tertiary pediatric centre from Imphal, Manipur, which fulfilled the diagnostic criteria for MIS-C as described by the WHO.¹⁰ The clinical overlap between MIS-C, Kawasaki's Disease (KD) and SARS-CoV2 serves as a diagnostic challenge. MIS-C and KD are both characterised by prominent cardiac involvement. There are few differentiating features between MIS-C & KD. KD usually presents in the younger age group, usually less than 5 years and is more commonly seen in Asians.^{7,11,12} MIS-C is usually seen in the older age group (8-9 years) and present with prominent gastro-intestinal symptoms. Laboratory findings include lymphopenia and thrombocytopenia, which are not common in KD. MIS-C and SARS-CoV-2 have similar presenting signs and symptoms with the exception of mucocutaneous findings seen in MIS-C. However, MIS-C is usually seen in a previously well child and majority test positive for SARS-CoV-2 antibody.^{5,7} Differentiation of MIS-C from SARS-CoV-2 is essential for management.

Since the pathophysiology and mechanism of abnormal immune response remains poorly understood, the management is mainly based on its phenotypic similarity to KD. Current management of MIS-C is primarily with immunomodulators and supportive care. Intravenous immunoglobulin (IVIG) is most commonly used with or without corticosteroids, generally yielding favourable outcomes.^{12,13} In our case, Inj. Methylprednisolone was started initially due its reported modest benefit in reduction in the use of inotropic support, mechanical ventilation and disease severity.^{14,15} In children with MIS-C with cardiovascular involvement, treatment with CS was also reportedly associated with faster normalization of left ventricular ejection fraction, fever, laboratory analysis, and shorter ICU than IVIG-treated patients.¹⁶

Since cardiovascular complications especially coronary-artery aneurysm is an important overlapping feature of both MIS-C and Kawasaki's disease, intravenous immune globulin (IVIG), the proven treatment for Kawasaki's disease, and which has been widely adopted as an essential therapy had been added.¹⁷ Our case had also exhibited dilated atria and coronary arteries, these showed improvements on follow up. Although many children may require critical care, majority of the children usually recover without sequelae. The cardiac manifestations include left ventricular dysfunction, coronary dilation and aneurysms and cardiogenic shock. Even though they are largely treatable, they can be potentially life-threatening if there is delay in diagnosis and management.^{9,15} Belhadier. Our patient had hypotension at admission requiring inotropic support (Inj Epinephrine) for stabilization. In MIS-C, strong suspicion, early recognition and prompt management is required to mitigate the adverse outcomes.

III. Conclusion

MIS-C has emerged as an important complication of SARS-CoV-2 infection among children. Severely affected children have been reported multiorgan failure and shock coupled with intense inflammation. As MIS-C includes a broad spectrum of illnesses with overlap of symptoms with other diseases, until a diagnostic test is developed, clinicians will face difficult treatment decisions when they encounter a wider group of inflammatory disease that occur after COVID infection than those identified by WHO criteria. Given the rapid emergence of MIS-C during the COVID-19 pandemic, clinicians should be more vigilant with adequate counselling to the caregivers to look for danger signs to prevent complications.

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