JK SCIENCE pISSN: 0972-1177

EDITORIAL

Multisystem Inflammatory Syndrome in Children

Ravinder K Gupta, Rohit Singh

Coronavirus disease 2019 (COVID-19), is a contagious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It is also termed as acute manageable immunogenic thrombogenic inflammatory contagious novel viral disease. Majority of children are asymptomatic or mildly symptomatic (1,2). Multisystem inflammatory syndrome in children (MIS-C) or pediatric inflammatory multisystem syndrome (PIMS / PIMS-TS), is a rare systemic illness causing persistent fever and extreme inflammation following exposure to SARS-CoV-2. In children who go on to develop MIS-C, some organs and tissues such as the heart, lungs, blood vessels, kidneys, digestive system, brain, skin or eyes become severely inflamed. Signs and symptoms depend on which areas of the body are affected (1-3).

Multisystem inflammatory syndrome in children (MIS-C) was first identified in April 2020, by doctors at children's hospitals in the United States and the United Kingdom. The predominant clinical findings were persistent fever, marked abdominal symptoms, cytokine storm, myocardial dysfunction and cardiogenic shock with left ventricular dysfunction, reminiscent of toxic shock syndrome (TSS) or Kawasaki disease shock syndrome (KDSS) and requiring ICU care. Other clinical findings such as conjunctival injection, oral mucosal changes and rash, features that are overlapping with TSS and incomplete Kawasaki disease (KD) were seen. Since mucocutaneous findings are present in KD, and because patients with MIS-C sometimes developed mild coronary artery dilation, diagnostic confusion initially led some clinicians to conclude that the two conditions were the same (4).

There is evidence of severe immune dysregulation, inflammation and hyper cytokinemia in the periphery and lungs of patients with severe COVID-19. There is increased levels of tumour necrosis factor (TNF)-á, interleukin (IL)-1â, IL-6, IL-18, IL-10, monocyte chemo attractant protein-1 (MCP-1) and interferon (IFN)-ã-induced protein (IP-10) or CXCL10. There is hyperactivation of the coagulant cascade and a relatively exhausted anticoagulant and fibrinolytic system with increased levels of D-dimer; evidence of microthrombi in large and small blood vessels and disseminated intravascular coagulation (DIC).

The occurrence of pediatric hyperinflammatory syndrome triggered by COVID-19 roughly 2-6 weeks after the inciting event oftentimes results in negative PCRs and serology, making diagnosis particularly challenging. Many children have often developed antibodies to SARS-CoV-2. In contrast to acute COVID-19, most children have gastrointestinal symptoms, such as diarrhoea, vomiting, and intense abdominal pain (mimicking appendicitis). Some Kawasaki-like symptoms that may be present (especially in children under the age of 5) include mucosal changes around the mouth ("strawberry tongue", cracked lips, etc.), red eyes, rash, red or swollen hands and feet, and enlarged lymph nodes. Various neurological disturbances such as encephalopathy, stroke,

Department of Paediatrics, Acharya Shri Chander College of Medical Sciences (ASCOMS) Jammu, Jammu and Kashmir, India

Correspondence to: Dr. Ravinder K Gupta, Professor and HOD, Department of Paediatrics, Acharya Shri Chander College of Medical Sciences (ASCOMS) Jammu, Jammu and Kashmir, India

Published Online First: 10 June 2021

Open Access at: https://www.jkscience.org/

Cite this article as: Gupta RK, Singh R. Multisystem inflammatory syndrome in children. JK Science 2021;23(2):58-59.

meningitis and Guillain-Barre Syndrome are seen. Acute heart failure is common in the form of left ventricular dysfunction. Respiratory symptoms are less common. Coronary artery abnormalities, such as dilatation, are frequent and many children have developed coronary artery aneurysms (3-6).

Inflammatory markers generally include raised ESR, CRP, procalcitonin, ferritin, and IL6. Thrombocytopenia, impaired coagulopathy, increased levels of D-dimer and fibrinogen are also seen. Pleural effusion, pericardial effusion, and ascites have also been reported (6,7).

Differences with respect to Kawasaki disease include frequent presentation with gastrointestinal symptoms. Neurological involvement also appears to be relatively frequent. It often affects older children, whereas KD usually occurs before the age of five. Multiorgan disease appears to be more frequent. Features of macrophage activation syndrome appear to be more frequent than in KD (8). Laboratory findings that are not usually encountered in KD include very high levels of ventricular natriuretic peptide (a marker of heart failure), thrombocytopenia, lymphopenia, higher CRP levels and very high troponin levels. The cardiac biomarkers (NT pro BNP, Troponin and CPK-MB) are of course indicative of myocarditis and can be used to predict clinical deterioration and shock (5,6). Bacterial sepsis, staphylococcal and streptococcal shock, appendicitis and mesenteric adenitis and infections associated with myocarditis need to be kept in mind.

Rarely, some adults develop signs and symptoms weeks after COVID 19 infection similar to MIS-C and is called as multisystem inflammatory syndrome in adults (MIS-A) and a diagnostic or antibody test for COVID-19 can help confirm current or past infection (6).

Management tends to be broadly based on anti-inflammatory medications, inotropic or vasoactive agents, treatment of shock, and prevention of thrombosis. Most children have received intravenous immunoglobulin (IVIG) and steroids at various doses. In few cases, cytokine blockers to inhibit production of IL-6 (tocilizumab) or IL-1 (anakinra) or TNF-á-inhibitors (infliximab) have been used as a supplemental therapy (3-7).

Patients diagnosed with MIS-C should have close outpatient pediatric cardiology follow-up starting 1 to 2 weeks after discharge. Primary care follow-up is recommended for all patients.

Further studies and longer surveillance of patients diagnosed with MIS-C is required to improve our diagnostic, treatment and surveillance criteria.

References

1. Meena J, Yadav J, Saini L, Yadav A, Kumar J. Clinical features and outcome of SARS-CoV-2 infection in children: a systematic review and meta-analysis. *Indian Pediatr* 2020;57(9):820-26.
2. Feldstein LR, Rose EB, Horwitz SM, Collins JP, Newhams MM, Son MBF, *et al*. Multisystem inflammatory syndrome in U.S. children and adolescents. *N Engl J Med* 2020;383(4):334-46.
3. Jiang L, Tang K, Levin M, Irfan O, Morris SK, Wilson K, *et al*. COVID-19 and multisystem inflammatory syndrome in children and adolescents. *Lancet Infect Dis* 2020;20(11):e276-88.
4. Dhanalakshmi K, Venkataraman A, Balasubramanian S, Madhusudan M, Amperayani S, Putilibai S, *et al*. Epidemiological and clinical profile of pediatric inflammatory multisystem syndrome - temporally associated with SARS-CoV-2 (PIMS-TS) in Indian children. *Indian Pediatr* 2020;57(11):1010-14.
5. Rauf A, Vijayan A, John ST, Krishnan R, Latheef A. Multisystem inflammatory syndrome with features of atypical Kawasaki disease during COVID-19 pandemic. *Indian J Pediatr* 2020;87(9):745-47.
6. Dufort EM, Koumans EH, Chow EJ, Rosenthal EM, Muse A, Rowlands J, *et al*. Multisystem inflammatory syndrome in children in New York state. *N Engl J Med* 2020;383(4):347-58.
7. Sundaram TG, Gupta L. Hyperinflammatory syndrome in children related to Covid-19. *Indian J Rheumatol* 2021;16:73-78.
8. Bhatia A, Gupta L, Agarwal V. COVID-19 and Rheumatology. *JK Science* 2021;23(1):1-2.