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Case Report
Inflammatory

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Multisystem Inflammatory Syndrome in Children (MIS-C): New challenges of a new era

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In the background of a sudden surge of coronavirus disease 2019 (COVID-19) cases, reports of the multisystem inflammatory syndrome in children from different parts of the globe are a matter of concern for physicians. We report a similar case presenting with persisting fever, rashes, bulbar conjunctivitis, abdominal pain, respiratory difficulty, and shock. Initial reports suggestive of high inflammatory markers, neutrophilic leucocytosis, high d-dimer, transaminitis, and found to have COVID 19 IgG antibodies positive in high titer. The echo at the bedside is suggestive of poor LV function with normal coronaries. Managed successfully in PICU with non-invasive ventilation support, ionotropy, aspirin, IVIG, and steroids and discharged. Early referral, a high index of suspicion, prompt recognition of shock, and early management by steroids and intravenous immunoglobulin (IVIG) may bring success.

Keywords: MISC, Multisystem inflammatory syndrome in children, COVID-19, LV dysfunction, Children

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Introduction

Case reports have appeared describing children with unusual febrile illnesses that have features of Kawasaki disease, [1] toxic shock syndrome,[2] acute abdominal symptoms, and encephalopathy, along with elevated inflammatory markers, and multisystem involvement in the background of this COVID 19 pandemic [3-5].

COVID-19 infection in children is less severe and has lesser mortality, compared to adults, so often missed, so the understanding of the epidemiology and clinical course of the multisystem inflammatory syndrome in children (MIS-C) and its association with COVID-19 is the need of the hour for public health implications of the syndrome.

Case Report

An 11 year previously well male child presented with persisting fever for 6-7 days, abdominal pain, and vomiting for 3 days generalized maculopapular erythematous rash and conjunctival congestion for 3 days, and breathing difficulty for 1 day. At presentation he was irritable, in hypotensive shock (BP=68/35(49) mm Hg) and hypoxemic (PAO2=55), so shifted to PICU immediately.

The shock was managed by fluid boluses and ionotropy, as bedside ultrasound was suggestive of poor cardiac contractility (EF=35%). He required non-invasive ventilation at IPAP of 12 and EPAP of 6 in ST mode, which improved oxygenation. In suspicion of the hyperinflammatory syndrome, IVIG (1gm/kg) and steroids were started along with broad-spectrum IV antibiotics, judicious fluid therapy, and other supportive care.

There was moderate anemia (Hb-9gm %), neutrophilic leucocytosis (14,500,N-79%) and normal platelet count. Initial d-dimer was very high (3950ng/ml), high ferritin (485mg/dl), high CRP (55), high LDH (574), high lactate, ESR (110), hyponatremia (Na -125mmol/dl), transaminitis, albumin (3.1gm/dl). X-ray chest was suggestive of bilateral opacities ECG was normal. Gradually the patient responded to the ongoing treatment and bedside 2D echo was suggestive of improved ventricular function. The general condition of the patient improved gradually over the next 48 hours. RTPCR for COVID 19 was negative but IgG antibodies were positive in high titer. Close monitoring of d-dimer showed decreasing titer as it came down to 1440ng/ml at 48 hours.

Fever subsided and other parameters also improved and the patient shifted out of intensive care. Blood C/S was sterile. ECHO was normal. Abdominal ultrasound was not suggestive of any thrombotic event. Steroids slowly tapered off over the next 4weeks. The patient is doing well on follow up.

Discussion

Multisystem inflammatory syndrome in children (MISC) is a condition mimicking TSS and Kawasaki disease in the background of the surge in cases of COIVID-19 is being reported from many parts of the world is a matter of concern for the treating pediatricians. The preliminary case definition in Children and adolescents (0-19 years) with fever $\geq$3 days and two of the following [6,7].

01. Rash or bilateral non-purulent conjunctivitis or mucocutaneous inflammation signs (oral, hands, or feet).
02. Hypotension or shock.
03. Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated troponin/NT-proBNP),
04. Evidence of coagulopathy (by PT, PTT, elevated d-Dimers).
05. Acute gastrointestinal symptoms (diarrhea, vomiting, or abdominal pain).

AND elevated markers of inflammation such as raised ESR, CRP or procalcitonin AND, no other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes AND, evidence of COVID-19 (RT-PCR, antigen testing or serology positive) or likely contact with patients with COVID-19. Clusters of children from the UK with this inflammatory syndrome had an acute febrile illness with evidence of single or multi-organ dysfunction. Laboratory features were neutrophilia, elevated CRP and clinical features included abdominal pain, gastrointestinal symptoms, myocarditis, and shock [8]. In our case, we have a persisting fever, non-purulent conjunctivitis, generalized rash, cardiogenic shock, high d-dimer, abdominal pain, high inflammatory markers with IgG antibody positivity which clinches the diagnosis of MISC. In the cluster of cases from the UK, common microbial causes were excluded and SARS-CoV-2 PCR testing was positive in a few cases, while serological tests (possible preceding SARS-CoV-2 infection) were positive in some cases [9].

In the present case, RT PCR was negative but the antibody test was positive. The patient hailed from a COVID hotspot area. Hence, past asymptomatic infection in the child was a possibility. In a presentation, we considered atypical KD, TSS, septic shock, and MAS with a background of vasculitis as the other differentials. ANA and vasculitis panel was negative. As the general condition of the child was deteriorating very fast, we considered pulse dose steroids and IVIG very early in the course. After which there was a remarkable improvement in cardiac function and shock. Invasive ventilation could also be avoided. As general condition improved remarkably and no thrombosis on detailed ultrasound doppler, we postponed our plan for low molecular weight heparin therapy and monitored the d-dimer closely which subsided over the next 72 hours. There may be an association between the COVID 19 antibodies and such type of hyperinflammatory conditions mimicking KD or TSS which needs further research work but awareness of such condition will ease the management.

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