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Multisystem Inflammatory Syndrome in Children [MIS-C] - A case report

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ABSTRACT

After the appearance of COVID 19 infection, surging number of nations reported children with inflammatory syndrome, presented with clinical features that overlaps with Kawasaki disease, Toxic shock syndrome, Macrophage Activation Syndrome. Intravenous immunoglobulin with or without steroid or aspirin is the preferred management for MIS-C. Here we report a case of 6-y-old girl who was managed by intravenous steroids alone. On examination, the child had bilateral Conjunctival congestion with persisting high grade fever. Initial investigations exhibited elevated inflammatory parameters such as ESR and CRP. Echocardiography displayed grade 2 Mitral regurgitation and grade 2-3 tricuspid regurgitation with mild PAH. Cardiac isoenzymes CK-MB was also elevated, suggesting myocardial cell wall injury. She was treated with antibiotics, steroids and antipyretic. RT PCR for SARS-CoV-2 was negative but antibody test was positive. Her clinical condition improved and became afebrile from day 5, inflammatory parameters were decreased and was discharged after 11 days of hospital stay.

INTRODUCTION

In children, COVID 19 is usually mild and has lesser mortality. But in rare cases, children can be seriously affected and may show a different clinical profile as compared to infected adult. National Health System (NHS) of United Kingdom and Pediatric Intensive Care Society (PICS) documented presentation of around 20 children with almost similar features of incomplete Kawasaki disease or Toxic shock syndrome.[1] Since then, many reports have been documented across the world with similar presentations.[2,3,4] This condition is termed as multisystem inflammatory syndrome in children [MIS-C] also referred to as pediatric inflammatory multisystem syndrome [PMIS] or pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2. Usual timing of onset of MIS-C symptoms is two to six weeks; however rarely, symptoms were shown after six weeks of acute SARS-CoV-2 infection. In some children, the clinical manifestation may almost be similar to complete or incomplete Kawasaki Disease [KD] with coronary artery aneurysms and extracardiac manifestations. But epidemiology differs from classic KD, older children and adolescents were in fact the most affected population in pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2. The rates of MIS-C varies with race and ethnicity; Black and Hispanic children accounts for large number of MIS-C cases than Asian children. Some case series on MIS-C [5,6,7] revealed that rates of MIS-C in black children was 25-45%, 30-45% in Hispanic children while only 15-25% in Asian children. Besides hand and foot swelling, strawberry tongue, non-exudative conjunctivitis, rash and unilateral significant lymphadenopathy, MIS-C can present with multiorgan failure including neurologic involvement, hyperferritinemia and cardiogenic or vasoplegic shock. Also GI Manifestation such as vomiting, diarrhea and severe abdominal pain were reported [8].

Since fever in children is a common presentation and the recent exposure to covid -19 in kids have been high, health care professionals are in a dire emergency. Patients who are presented with part of but not all features of MIS-C have low index of suspicion, inflammation screening including a complete blood count (CBC) and C-reactive protein (CRP) with SARS-CoV-2

PCR Testing and antibody testing should be considered in them. Patients who fulfill the case definition clinical features of MIS-C should undergo an extensive medical examination. As the patient who were initially be well with marked Laboratory workup may later display worsening symptoms and clinical deterioration, hence MIS-C specific discharge instructions with a Routine follow-up is recommended. [8]

CASE REPORT

Herein we report a case of 6 year old girl admitted with a 5 day history of persistent high grade fever along with vomiting referred from another Hospital. On physical examination, she was febrile, lethargic with bilateral conjunctival congestion but had no rashes or strawberry tongue like other MIS-C cases. There was no known contact to a COVID-19 patients. Real time PCR for SARS-CoV-2 was done during the hospital admission and did not detect SARS CoV-2 but antibody test results were positive. This indicated that the child was infected with COVID-19 sometime in the past. When inquired to her parents revealed that the child and her sibling had fever in past, but had no previous hospital admission as it subsided within two days. Alike other COVID-19 patients the D-dimer was highly elevated with normal ferritin. Vitals were stable with a temperature of 39°C. Complete blood count indicated neutrophilic leukocytosis [TLC - 11200/µL (N-84%, L-15%)] with normal platelet count (2.1 lakh/µL). Inflammatory parameters were high (CRP - 135.2 mg/L, ESR 68 mm/h,) and serum creatinine (0.6 mg/dl) and liver enzymes were normal (AST - 26 U/L, ALT- 22 U/L). Cardiac isoenzyme CK -MB was elevated, suggesting myocardial cell wall injury. Urine and blood cultures were obtained and were negative. On day 2 of illness, widal test was carried out to rule out typhoid, and it was negative. Echocardiogram revealed grade 2 Mitral regurgitation and grade 2-3 tricuspid regurgitation with mild Pulmonary Arterial Hypertension [PAH]. In view of ongoing pandemic these features suggest patient had MIS-C.

Since admission, the child received Paracetamol suppository [250mg every 6 hour] and continued till day 5th since child continued to have high grade fever spikes up to day 4. The antibiotic therapy was also initiated on the first day itself with intravenous Amikacin [300mg OD]. And then intravenous Cefoperazone - Sulbactum combination were added on the next day. Tobramycin eye drop was put on to the therapy considering the Conjunctival congestion on both eyes. To resolve inflammatory state associated with MIS-C intravenous Methyl prednisolone [40mg OD] was started and then converted to syrup Prednisolone after 6 days. Meanwhile on day 3, the child had diarrhoea and so was advised to administer ORS along with soft diet. As the symptoms persisted and inflammatory parameters remained high, IV immunoglobulin was suggested. By the course of time, child had dramatically improved, her inflammatory parameters and temperature reduced and hence steroids was continued without the addition of immunoglobulins. The child remained clinically well, steroid was slowly tapered, antibiotics stopped and discharged on day 11 with oral steroid for 5 days; was also advised for review visit along with ECHO, CBC, CRP, CKMB. At follow-up visit after 13 days, the patient had normal CK-MB (25 IU/L), increased inflammatory parameters (ESR-28mm/h and CRP- 12.9mg/L), ECHO showed coronary artery dilatation. Hence added aspirin 75mg in addition to oral steroid (0.5mg/kg/day). On the next OP visit after 2 weeks, the laboratory and radiological reports showed improvement so steroid was tapered but aspirin was continued for 2 months.

DISCUSSION

Newer diseases may create greater challenge to health care teams for its diagnosis and management. SARS-CoV-2, recognized on December 2019 in China is now been spread all over the world. There is increasing concern of SARS-CoV-2 related inflammatory syndrome, a new febrile pediatric entity characterized by systemic hyperinflammation, abdominal pain, GI symptoms and multiorgan involvement particularly in children. Various designations have been proposed for this syndrome including multisystem syndrome in children [MIS-C], pediatric inflammatory multisystem syndrome [PMIS] or pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2.[9] Clinical profile of MIS-C overlaps with Kawasaki disease, Toxic shock syndrome and Macrophage Activation Syndrome. [10]

Previously adenovirus and New Haven corona virus acted as a triggering factor for KD. But recently Kawasaki disease like cases due to SARS-CoV-2 were reported across the world which excluded common microbial agents.[2] Absence of viral RNA in patient doesn't become a barrier in diagnosis as the syndrome may be developed even after viral clearance from upper airways. After 1-2 weeks of infection antibodies will be formed. IgM antibodies are formed during first period of infection and slowly disappear after few weeks, meantime IgG antibodies dominates over IgM. Thus high level of IgM antibodies indicate that infection may be occurred few weeks back or even months back.[11] In the present case, Urine culture, blood culture and RT PCR were negative on admission but antibody titers to SARS-CoV-2 was positive. Hence past asymptomatic COVID 19 infection was clearly recognized.

MIS-C and kawasaki diseases have some dissimilarities too. kawasaki disease is more commonly seen in children less than 5 years of age whereas MIS-C is more common in children older than 5 years.[12]. Most of the studies reported that median age of presentation of MISC to be higher than 5 years.[9,13] Asian population have highest incidence of KD but MIS-C is rare in this population.[10] Also left ventricular dysfunction is a main clinical feature in MIS-C than KD. [12] Cardiac dysfunction was seen nearly half of the patients with MIS-C. [10] Myocardial involvement may vary from moderate to very severe condition ; much greater correlation than with KD or KD shock syndrome.[9] The lab parameters have greater similarity with Macrophage Activation Syndrome and Toxic shock syndrome than KD [elevation of D-dimer, ferritin, triglycerides]. [9,14] In current case ,Cardiac isoenzyme CK-MB were elevated, suggesting myocardial cell wall injury. Studies conducted in adult population suggest that high D-dimer is linked with poorer outcome. Also raised level of CRP and IL-6 are associated with severity and mortality.[10,15] The present case also had almost similar laboratory parameters and clinical profile. A multicenter observational study in UK revealed that clinical presentations and treatment varies in each cases. The survival rate is high but the long term effect of MIS-C is unknown.[7] Most patients diagnosed with syndrome can recover quickly if appropriate therapy is initiated early. Intravenous immunoglobulin with or without steroid or aspirin is the preferred management; Intravenous immunoglobulin as first line agent whereas regular dose or pulse methyl prednisolone as second line therapy. [12] As the index patient responded positively to methyl prednisolone therapy, intravenous immunoglobulin was not used in our case. As long term outcomes are not known, children need long term follow up and monitoring of cardiac function.

CONCLUSION

In India, the younger children remain most vulnerable to COVID-19 and its variants since they are not yet included in vaccination section. So health care team should be aware of this new clinical syndrome associated with SARS-CoV-2 which shows similar characteristics of kawasaki disease. A great care should be given to identify this syndrome early in the course of illness so that a favorable outcome can be obtained by providing appropriate therapy. Also healthcare team should generate awareness and confidence among public to vaccinate their children to avoid further complications.

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