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Case Report

Post- COVID-19 multisystem inflammatory syndrome in children

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ABSTRACT

Background: COVID-19 is a severe acute respiratory infection affecting worldwide population. There are many cases of complications after the COVID exposure occurring nowadays. One among is Post-COVID-19 Multisystem Inflammatory Syndrome in Children (MIS-C). As per CDC report till March 1, 2021, 2617 cases of MIS-C were meeting the definite case criteria and among 33 death cases were reported. Here we report a case of COVID-19 associated Multi-system inflammatory syndrome in a child (MIS-C) interpreted with WHO case definition criteria.

Case Description: The patient was a 7-year-old boy, with initial presentation of moderate fever, non-itchy red blanching rashes, breathlessness, later progressed to cardiogenic shock accompanied by positive SARS-CoV-2 antigen result.

Management: The emergency cardiogenic shock treatment protocol was followed with initial stabilization and resuscitation strategy. He was successfully managed by three days of IV Immunoglobulin 2g/kgand Methylprednisolone 2mg/kg/day therapy along with other supportive treatments. The patient was discharged after 20 days of hospital stay with improved health condition.

Conclusions: Our case report will strengthen the exposure-outcome relations between the coronavirus infection and MIS-C, moreover the strategies carried out in our case will be a future direction for the effective management of MIS-C.

1. Introduction

Coronavirus disease 2019 (COVID-19) is a global pandemic that has been spreading worldwide and has affected about 224 countries. As of 25 March 2021, there are more than 124 million confirmed cases of COVID-19 and over 2,734,374 deaths.[1] The epidemiological data from the countries like Asia, Europe, North America reveals that the paediatric population was affected by COVID-19 at a rate of 2.1–7.8%. There has been an increased occurrence of COVID-19 associated complications in paediatrics, one among is MIS-C which is mostly developed, two to four weeks after the corona virus exposure.[2]

According to Centres for Disease Control (CDC), "MIS-C may be outlined as the manifestation of fever with increased inflammatory markers like C-reactive protein, ESR, Procalcitonin, D-dimer, LDH, IL-6, Neutrophils, weakened lymphocytes andis one of the severe conditions that requires emergency hospital admission with involvement of multiple organ (≥2) including heart, kidney, lungs, skin, nerve cells and epithelial duct organs". If all the above symptoms are linked with positive Real-time reverse transcriptase-polymerase chain reaction (RT-PCR)/Ig G/antigen test for severe acute respiratory syndrome (SARS)-CoV-2 or has a COVID-19 exposure within the past 4 weeks of symptom onset, then it can be

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confirmed as Post-COVID MIS-C.[3] As per the CDC report until March one, 2021, the overall range of MIS-C cases meeting the definite case criteria was concerning 2617 and thirty-three death cases were reported. The cases principally reported were in paediatric population ageing between one to fourteen years with bigger incidence in male cluster (59%).[4] Here we report a case of a child developing MIS after the COVID-19 exposure.

2. Case Report

A 7-year-old boy had admitted to Paediatric Department, KIMS Hubli, India with complaints of fever of moderate degree which was insidious in onset, gradually progressive associated with non-itchy red blanching type of rashes started over trunk and then progressed to face in a descending pattern. He was also presented with icterus and generalised oedema, initially involved his lower limbs, and then progressed to whole of his body. So the child was admitted to nearby child care hospital, where he was given with Inj. Ceftriaxone 500mg IV BD, Inj. Lasix 10mg IV STAT, IVF $\frac{1}{2}$ DNS (50 ml/hour).

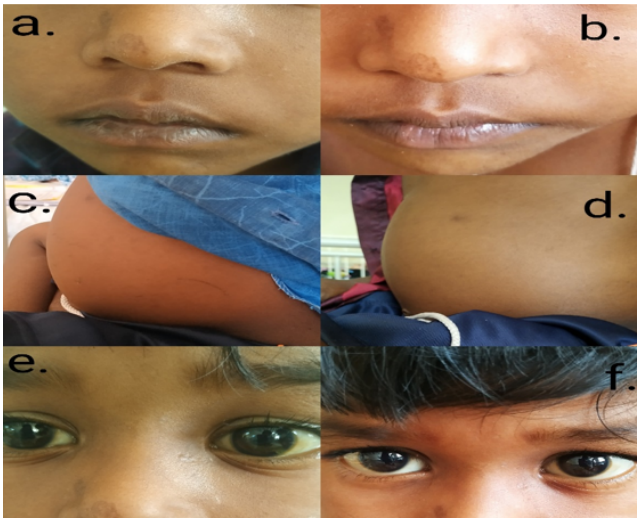

Fig. 1: a: Chapped lips (common feature of MIS-C and KD); **b:** Lips got normal after 10 days; **c:** Abdominal distension; **d:** Abdominal distension resolving after 10 days; **e:** Icterus; **f:** Icterus resolving after 10 days

But the boy was not maintaining his oxygen saturation, and therefore, he was immediately shifted to multispecialty hospital for better health care. Upon reaching the hospital, he developed hypotension (BP- 90/50 mm Hg), tachycardia (HR- 110bpm), poor saturation (SpO_2 - 92%) and his peripheral extremities were cold. Echocardiographs showed an impression of mild LV dysfunction, mild pericardial effusion with reduced left ventricular ejection fraction (40%). These observations made the provisional diagnosis as cardiogenic shock. So, as part of following the emergency cardiogenic shock treatment protocol, the initial stabilization and resuscitation strategy was initiated by the administration of 500ml IV Normal Saline and the child was ventilated non-invasively by the high flow nasal cannula for oxygen supply at a flow rate of 2L/kg/min. The vasopressor support was provided by administering 0.01 mg/kg of Inj. Adrenaline and after which, the patient got stabilized with 100% saturation on oxygen.

His abdominal ultra-sonogram imaging gave the picture of bilateral grade I renal parenchymal changes, mild hepatosplenomegaly with right mild and left minimal pleural effusion. Correlating USG Abdomen and 2-DECHO report with his initial clinical features gave the clear view of multiple organ failure in this patient. The patient's SARS-COV-2 IgG report was obtained to identify the aetiology and precipitating factor of MOF, which was positive (4.03), confirming the status of past infection with COVID-19virus. His D-Dimer (3410 ng/ml) and Ferritin (301.44 ng/ml) levels were also elevated.

All of his subjective and objective data depicted the strong evidence for the diagnosis of Post-COVID Multisystem Inflammatory Syndrome in this child. In view of managing the condition MIS, the child was treated by administering IV immunoglobulin 2g/kg and IV methylprednisolone 2 mg/kg/day for 3 days along with Lasix infusion and the antibiotics Inj. Doxycycline 4.4 mg/kg/day, Inj. Meropenem 20 mg/kg. Despite his present illness, he was transferred to a public hospital because of the financial crisis, where he was administered with 10 days of Inj. Ceftriaxone 75mg/kg/day, Tab. Prednisolone 2mg/kg/day, and Tab. Paracetamol. Five days after the initial presentation of his symptoms, he was symptomatically better with reduced abdominal distension as well as the icterus also got resolved. The 2-D ECHO report after 5 days showed that he regained his normal bilateral ventricular function with Left Ventricular Ejection Fraction (LVEF) of 60% and all his inflammatory marker came to its respective standard level. The child got discharged after 20 days of treatment in healthy status. A written informed consent was obtained from the parents/guardians of the patient for publication of case data and images.

3. Discussion

The severe acute respiratory syndrome coronavirus 2 affects all age ranges, but it has additional impact on geriatric as well as the patients with multiple diseases, because in aged patients with comorbid conditions like hypertension will have overexpression of ACE-2 receptor which is a binding site for corona virus, moreover ageing can dysregulate the innate immune response leading to the immunological dysfunction associated lung injury.[5] Newly, there have been reports of COVID-19 associated MIS in people less than twenty-one years of age.[6]

Table 1: Laboratory parameters taken on first, tenth, twentieth day of admission

Lab Parameters	Day 1 of admission	Day 10 of admission	Day 20 of admission
Creatinine (mg/dl)	**2.8**	1	0.8
Urea (mg/dl)	**87.2**	59	31
WBC (cells/cumm)	**12,000**	11,600	10,200
PLT (cells/cumm)	**80000**	281000	336000
D-Dimer(ng/ml)	**3410.4**	-	-
Ferritin (ng/ml)	**301.44**	**287**	146
CRP(Mgs/L)	**12**	7	7
Hb (gm %)	**10.2**	**7.4**	8.1
2D Echo- LVEF	**40%**	60%	-

Even though, there was many literature resources defining the criteria for Post-COVID MIS-C, we are correlating our case with WHO case definition criteria. It includes the ageing between 0-19 years, presented with initial symptoms of fever, elevated inflammatory markers for three days or more and any two of the following main features,

1. Rash/Bilateral non- purulent pink eye or mucocutaneous inflammation signs (oral, hands or feet)
2. Hypotension or shock
3. Features of myocardial dysfunction (including echocardiogram findings/ elevated troponin/ N-terminal protein/B- type natriuretic peptide)
4. Proofs of coagulopathy like elevated PT/INR, D-dimer
5. Acute GI issues

Additionally, the standard needs, a positive RT-PCR/antigen test/serology/any contact with patients having COVID-19.[7]

Here, in our case, the kid was meeting the points of criteriasuch as the initial symptoms of fever, elevated inflammatory markers (CRP, ESR) and the four main features, the presence of rashes, shock, LV dysfunction, elevated D-Dimer overlapping with positive SARS Cov-2 antigen result.

The first case of Post-COVID MISC was reported in April 2020, where the child was presented with fever, rashes, conjunctivitis, tachycardia and tachypnoea with positive RT-PCR result.[8] Along with these latest researches, our case report will strengthen the exposure-outcome relationship between COVID and MIS-C. There are multiple mechanisms explaining the pathogenesis of Post COVID MIS-C. The primary binding site of corona virus in human cell is ACE-2 and these receptors for SARS-Cov2 is mostly localized in the epithelium of lung, small intestine, kidney, liver, brain. The invasion and binding of virus to the ACE-2 receptors can trigger the innate immune response leading to immunological imbalance as well as cytokine storm. So this generates the way to hyper-inflammation through the release of circulatory cytokines including IL-6, IL-8, IL- 1ß, TNF-α, (MIP 1α,1ß), IF-α, IF-ϒ which then ends up with various hyper inflammation-induced tissue injuries like shock, multiple organ failure, respiratory distress syndrome.[2]

As the Post COVID MIS-C and Kawasaki disease shares similar clinical and diagnostic features, the management for MIS-C is mainly based on the standard treatment protocol for KD's.[5] The standard management for MIS-C is illustrated below. Correspondingly in our case, the patient was non-invasively ventilated and resuscitated using 500ml of IV NS along with Adrenaline for inotropic support. As per American College of Rheumatology guidelines for the MIS-C management, 1-2g/kg of IV immunoglobulin and low to moderate doses of glucocorticoids should be started as the first line immunomodulatory treatment in all paediatric patient with MIS and the treatment given in our patient was parallel to guideline directed recommendations. The glucocorticoids can suppress the hyper active innate immune reaction, thereby prevents the risk of shock progression. Aspirin at low dose should be given in MIS-C patients with elevated D-Dimer but in contrast to the guideline, aspirin was not added in this patient because his platelet count was less than 80,000 cells/cumm and its use is not recommended in cases of patients with low platelet count as well as he was showing the early signs of AKI.[9] Our case report will strengthen the exposure-outcome relations between corona virus infection and MIS-C, moreover the strategies carried out in our case will be a future direction for the effective management of MIS-C.

Children with signs of shock/sepsis/Kawasaki disease/MIS-C are thus advised to be put on the following treatment:-

3.1. Oxygen therapy

1. In children with emergency signs of ARDS, cyanosis, shock, consider advanced oxygen/ventilatory support, if child is not responding to standard oxygen therapy. Provide mechanical ventilation using tidal volume of 3-6ml/kg in children with poor breathing compliance/ 5-8ml/kg with better compliance at a target of plateau pressure <28cmH_2O

3.2. Fluid resuscitation

1. Consider 10-20 ml/kg of crystalloid fluid (ringer-lactate, normal saline, plasma- lyte B) as bolus in the first 30-60 minutes and the signs of fluid overload after each bolus should be monitored.

3.3. Vasopressor support

1. Consider vasopressors if the child has cold peripheries/elevated lactate level/HR <70 or >150 bpm/ lower urine output. Adrenaline is preferred primary treatment in children, consider noradrenaline if the shock isn't controlled even after normal dose of adrenaline.[10]

Consult paediatric ID specialist. Perform ECG, 2D-Echo, USG and send the samples for CBC, ESR, CRP, ferritin, D-dimer, SARS Cov2 RT-PCR or serology tests.[5]

3.4. Immunomodulatory treatment

1. Consider immunomodulatory treatment only after the confirmed diagnosis of MIS-C except in conditions of severe life-threatening complications. Administer 1-2g/kg of IV immunoglobulin with three days of pulse glucocorticoid (1-2 mg/kg) therapy under close monitoring of heart function and fluid status. Consider Anakinra > 4mg/kg/day in cases of refractory or contraindication to the former immunomodulatory treatment

3.5. Antiplatelet therapy

1. Consider 3-5 mg/kg/day; max 81mg/day of aspirin in children with platelet count ≥ 450,000/μL. Use should be avoided in condition with platelet count ≤ 80,000/μL.[9]

4. Conclusions

The epidemiological data shows that COVID-19 is affecting paediatric population at a rate of 2.1-7.8%. MIS-C is a complication which is occurred after the coronavirus exposure in most of the children. It can be managed by three days of IV IG (2g/kg) and Methylprednisolone 2mg/kg/day.

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6. Conflict of Interest

The author declares no potential conflicts of interest with respect to research, authorship, and/or publication of this article

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None

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