VOLUME - 10, ISSUE - 05, MAY- 2021 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Paediatrics

A RARE CASE OF MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN (MIS-C) TEMPORALLY RELATED TO COVID-19 IN A 2-MONTH-OLD INFANT WITH CARDIOVASCULAR AND NEUROLOGICAL INVOLVEMENT

Dr Deepa A Banker	Professor and Head, Department of Pediatrics, SMT NHL Municipal Medical College, Ahmedabad – 380006.
Dr Ishani Sarda*	2nd Year Resident, Department of Pediatrics, SMT NHL Municipal Medical College, Ahmedabad – 380006.*Corresponding Author
Dr Bhavdeep M Mungala	1st Year Resident, Department of Pediatrics, SMT NHL Municipal Medical College, Ahmedabad – 380006.
Dr Vimal T Maheshwari	1st Year Resident, Department of Pediatrics, SMT NHL Municipal Medical College, Ahmedabad – 380006.

ABSTRACT Multisystem Inflammatory syndrome in Children (MIS-C) temporally associated to Coronavirus disease 2019 (COVID-19) is a life-threatening condition. It has been commonly reported in the school going age group. We present a rare case of a two-month-old infant who was real time polymerase chain reaction (RT-PCR) positive for the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) fulfilling the World Health Organisation (WHO) criteria for MIS-C. Cardiac and inflammatory markers were raised at the time of admission with echocardiography showing biventricular dysfunction. Patient was treated with a course of intravenous immunoglobulin (IVIg) with rapid clinical improvement. During the course of hospital stay, patient developed generalised tonic-clonic seizures with magnetic resonance imaging (MRI) of the brain suggestive of viral encephalitis. Patient was vitally stable and symptom free by the 10th day of admission and subsequently discharged. This thus, represents a rare case of MIS-C in infancy having both cardiovascular and neurological affliction.

KEYWORDS : Multisystem Inflammatory Syndrome in Children (MIS-C), infant, COVID19

INTRODUCTION-

Coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a pandemic without parallel in human history. It has been associated with a myriad of systemic findings. As compared to adults, children are known to have less severe disease without need for hospitalisation in a majority [1]. However, one of the life-threatening manifestations seen in children is the Multisystem Inflammatory syndrome in Children (MIS-C) temporally associated to COVID-19. It is a pro-inflammatory condition of unclear pathophysiology leading to significant organ dysfunction and morbidity.1 Most of the cases have been described in children aged 8-11 years of age Further, data on MIS-C from India is sparse. Here, we present a case of a two-month-old infant who presented with cardiogenic shock fulfilling the criteria for MIS-C who was discharged after successful treatment.

CASE PRESENTATION-

A 2-month-old male child, weighing 4.6 kg, with nasopharyngeal swab RT-PCR positive for SARS-CoV-2, arrived in the emergency area, with a history of high grade fever of 7 days duration, breathing difficulty and reduced urinary output of 2 days duration. The child had an uneventful birth history (birth weight 2.75 kg, second order birth, full term), was completely immunized and had no significant past medical or family history. The child was drowsy with a Pediatric Glasgow Coma scale score of 12/15 and febrile (101.9F). The pulse was feeble with tachycardia of 174/min and a noninvasive blood pressure (NIBP) of 60 mmHg systolic. The child was tachypneic (74/min) with intercostal indrawing and not maintaining oxygen saturation on room air. Anterior fontanel was open and non-bulging. There was clinically no edema or rash. On chest auscultation there were crackles bilaterally. On examination of the abdomen, there was hepatomegaly of 2cm below the right costal margin. Child was moving all four limbs; signs of meningeal irritation and facial palsy were absent with normal bilaterally reactive pupils.

A bedside 2-dimensional echocardiography was done using a DC-40 portable ultrasound (Mindray Inc, Shenzhen, China) system. The study showed dilation of all four cardiac chambers with severe left ventricular dysfunction. Visualized portions of the coronary arteries on echocardiography appeared normal. There were moderate mitral and tricuspid regurgitation with a dilated inferior vena cava leading to a strong possibility of myocarditis. Chest X ray showed bilateral increased interstitial infiltrates.

Regarding laboratory parameters, D-dimer, ferritin, lactate dehydrogenase, creatine phosphokinase and procalcitonin were elevated. Antibody level in the serum for SARS-CoV-2 was significantly raised. Elevated creatine kinase-MB fraction (CK-MB; 97.97 ng/mL, reference value 0-6 ng/mL) and n-terminal pro-Brain natriuretic peptide (nT-ProBNP; >5000 pg/ml, reference <350 pg/ml) were suggestive of myocardial involvement. Blood urea nitrogen and hepatic enzymes were elevated with leukocytosis and anemia. Among the electrolytes, there was hypernatremia, hyperkalemia and hypocalcemia (table 1). Based on the above, in view of the clinical and lab picture, a diagnosis of MIS-C temporally related to COVID-19 was made based on the World health organization (WHO) case definition [3].

Table 1: Showing laboratory parameters at the time of admission

Investigations	Reference Range	Patient Result
Complete Blood Counts		
Total white blood cells	4,000-10,000/mm^3	14340
Hemoglobin	12-18 g/dL	9.3
Platelet count	150-4,50,000/mm^3	2,30,000
Biochemistry		
Random serum glucose	60-100 mg/dL	72
Serum creatinine	0.2-1.2 mg/dL	0.57
Serum urea	16-40 mg/dL	74.3
Serum total calcium	8.5-10.2 mg/dL	8.9
Serum sodium	135-145 mmol/L	153
Serum potassium	3.5-5.5 mmol/L	6
Serum chloride	98-107 mmol/L	112
Serum magnesium	1.7-2.6 mg/dL	2.90

Lactate dehydrogenase	115-225 UI/L	4196
Total serum bilirubin	0.2-1.3 mg/dL	1.80
Direct bilirubin		1.11
Serum Albumin	3.5-4.7 g/dL	3.7
Aspartate transaminase	<40-42 IU/L	1926
Alanine transaminase	<42 IU/L	721
Blood gases		
pH	7.35-7.45	7.42
Serum bicarbonate	22-26mEq/L	13.6
$PaCO_2$	35-45 mmHg	15.3
Coagulation profile		
Prothrombin time	10-11 seconds	80.2
Activated partial thromboplastin time	24-40 seconds	51.5
International Normalized Ratio	0.8-1	6.46
Inflammatory markers		
Erythrocyte sedimentation rate	Up to 20 mm in the 1st hour	28
C-reactive protein	<0.6 mg/dL	2.4
Serum Ferritin	10-500 ng/mL	1650
Cultures, serology		
Blood culture	No growth	No growth
Urine culture	No growth	No growth
Other Investigations		
Hematocrit	36-55%	29.6
Ionised calcium	1.22-1.44 mmol/L	0.31
D-dimer	<500 ng/dL	15.19
Fibrinogen	100-400 mg/dL	40
Procalcitonin	<0.05 mcg/L	2.02
Serum Lactate	0.5-2.0 mmol/L	8.6
Interleukin-6	1-5 pg/ml	7.4
Troponin-I	<2.0 ng/L	0.784
Creatinine Kinase-MB fraction	<25 U/L	97.97
N-Terminal pro-Brain Natriuretic Peptide	300-450 pg/ml	5000
Vitamin B12	>200 pg/ml	233
Vitamin D	>20 ng/ml	15.32
Serum Iron	50-120	252
Arterial partial pressure of oxygen	75-100 mmHg	183
Arterial oxygen saturation	92-99%	99.7
Cov 2T Antibody	0-1	7.34
Triglycerides	<100 mg/dL	118
CSF analysis		
Appearance	Clear	Clear, colourless
Total counts	<5/mm3	5
Polymorph cells	<25%	20%

Patient was put on inotropic support (dobutamine at 10 mcg/kg/min and noradrenaline at 0.05 mg/kg/min), steroids (methylprednisolone at 1 mg/kg/day for 5 days followed by dexamethasone at 0.2 mg/kg/day), intravenous immunoglobulin (IVIg) (2 g/kg in 24 hours followed by 1 g/kg for 5 days), vitamin K, antibiotics (meropenem, vancomycin and fluconazole), electrolyte correction (sodium and calcium), blood and blood products transfusion along with diuretics. With the same therapy there was significant improvement and by 72 hours of admission, there was no requirement of inotrope support and child was afebrile without tachypnea and tachycardia. A repeat echocardiography on the third day of admission showed a normal biventricular function. High-resolution computed tomography (HRCT) of the chest was not significant for findings related to COVID-19. Further, patient also developed generalized tonic-clonic seizures on the third day of admission which were treated with anti-epileptics. Cerebrospinal fluid (CSF) examination including analysis for herpes simplex (HSV) was normal. A magnetic resonance imaging (MRI) of the brain without contrast showed areas of diffusion restriction with T2/FLAIR hyperintensity in corpus callosum (predominantly in splenium), subcortical and periventricular deep white matter in bilateral fronto-parieto-occipital region and in bilateral cerebellar hemisphere with a possibility of viral encephalitis) (figure 1).

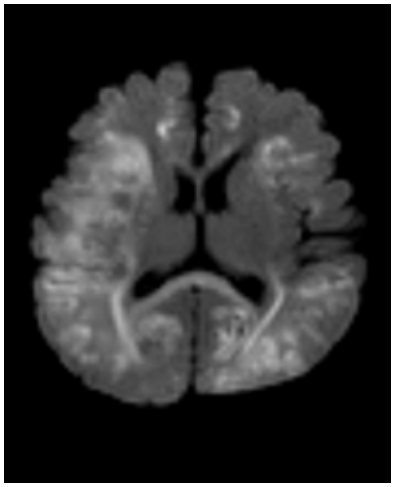

Figure 1: Axial diffusion weighted magnetic resonance imaging sequence showing diffusion restriction in bilateral fronto-parietal region and splenium of corpus callosum

Patient responded well to antiepileptics and no convulsion episode was noted. Child was vitally stable with normal blood pressure and no signs of raised intracranial tension. Enteral feeding was initiated on the sixth day of admission with expressed breast milk via nasogastric tube and volume was gradually increased. Child tolerated all feeds and was shifted to breastfeeding on day 10 of admission. Weight gain was present. Patient was discharged ten days after admission, with stable vitals and normal neurological and cardio-respiratory status, on oral anti-epileptics, supplements and breastfeeding.

DISCUSSION

MIS-C has been well reported during the pandemic. The WHO case definition for MIS-C temporally related to COVID-19 requires fulfilment of the following points [3]. Patients must be between the ages of 0-19 years; have fever of at least three days duration; have elevated markers of inflammation (such as erythrocyte sedimentation rate, C-reactive protein, or procalcitonin); have no other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes; have evidence of COVID-19 RT-PCR, antigen test or serology positive), or likely contact with patients with COVID-19; and at least two of five organ dysfunction parameters. These five are - Rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammation signs (oral, hands or feet); Hypotension or shock; Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponin/NT-proBNP); Evidence of coagulopathy (by PT, PTT, elevated d-Dimer); Acute gastrointestinal problems (diarrhea, vomiting, or abdominal pain).

The present case satisfied all the disease definitions. The largest meta-analysis on MIS-C related to COVID-19 covering 662 patients from 39 observational studies reported a mean age of 9.3±0.5 years [2]. In the largest cohort of MIS-C from Europe with 268 patients, only 7.3% patients were <1 year old [4]. This case thus, falls into a relatively uncommon subset where the child is only 2 months old. The main organ system involvement in this child was cardiovascular. The child presented in cardiogenic shock with depressed left ventricular

ejection fraction. The cardiac involvement in MIS-C has now been well studied and compared to Kawasaki disease (KD). As shown from data from an echocardiographic study of, as compared to classical KD, the coronaries appear largely to be spared in MIS-C with predominant left ventricular dysfunction [5]. The same was true for our case as well. As per data from a large review of cardiovascular manifestations in MIS-C related to COVID-19,6 shock was present in 50-80% patients, left ventricular dysfunction in 51-76% patients and elevated cardiac enzymes in 68-95% patients. The pathophysiology of cardiac dysfunction in MIS-C has been generally attributed to a 'cytokine storm' leading onto endothelial dysfunction, activation of complement and coagulation cascades and direct myocardial injury [6].

Neurological involvement in MIS-C is uncommon. A review of various studies found an incidence of 4-30% of neurological complications with the predominant entity being meningoencephalitis [7].The pathophysiology of the same is still unclear, but hinges on the proinflammatory cytokine storm mechanism [7]. The same review also pointed out the nature of the non-specific CSF and MRI findings in patients of MIS-C as found in our case. However, a case report of a 33-month-old child with neurological manifestations of MIS-C with MRI findings of bilateral thalamic findings is similar to the present case with a favorable response to IVIg [8]. A case series by Abdel-Mannan et al also found changes in the splenium of the corpus callosum similar to the present case [9].

CONCLUSION-

Despite children being less affected from COVID-19 infection than adults, MIS-C temporally related to COVID-19 infection represents both a diagnostic and therapeutic challenge. The myriad of manifestations of MIS-C must be kept in mind in the approach to a sick child with COVID-19 infection, as a rapid diagnosis and early institution of IVIg therapy can be lifesaving.

REFERENCES:

1. Dhochak, N., Singhal, T., Kabra, S. K., & Lodha, R. (2020). Pathophysiology of COVID-19: why children fare better than adults?. The Indian Journal of Pediatrics, 87, 537-546.
2. Ahmed, M., Advani, S., Moreira, A., Zoretic, S., Martinez, J., Chorath, K., ... & Moreira, A. (2020). Multisystem inflammatory syndrome in children: A systematic review. EClinicalMedicine, 26, 100527.
3. World Health Organization (WHO). Multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19. WHO Scientific Brief. Geneva. (2020). Accessed: 15 May 2020. https://www.who.int/newsroom/commentaries/detail/multisystem-inflammator y-syndrome-in-children-and-adolescents-with-covid-19
4. Valverde, I., Singh, Y., Sanchez-de-Toledo, J., Theocharis, P., Chikermane, A., Di Filippo, S., ... & Miller, O. (2021). AEPC COVID-19 Rapid Response Team. Acute cardiovascular manifestations in 286 children with multisystem inflammatory syndrome associated with COVID-19 infection in Europe. Circulation, 143(1), 21-32.
5. Matsubara, D., Kauffman, H. L., Wang, Y., Calderon-Anyosa, R., Nadaraj, S., Elias, M. D., ... & Banerjee, A. (2020). Echocardiographic findings in pediatric multisystem inflammatory syndrome associated with COVID-19 in the United States. Journal of the American College of Cardiology, 76(17), 1947-1961.
6. Alsaied, T., Tremoulet, A. H., Burns, J. C., Saidi, A., Dionne, A., Lang, S. M., ... & Friedman, K. G. (2021). Review of cardiac involvement in multisystem inflammatory syndrome in children. Circulation, 143(1), 78-88.
7. Chen, T. H. (2020). Neurological involvement associated with COVID-19 infection in children. Journal of the neurological sciences, 418.
8. Abel, D., Shen, M. Y., Abid, Z., Hennigan, C., Boneparth, A., Miller, E. H., ... & Bain, J. M. (2020). Encephalopathy and bilateral thalamic lesions in a child with MIS-C associated with COVID-19. Neurology.
9. Abdel-Mannan, O., Eyre, M., Löbel, U., Bamford, A., Eltze, C., Hameed, B., ... & Hacohen, Y. (2020). Neurologic and radiographic findings associated with COVID-19 infection in children. JAMA neurology, 77(11), 1440-1445.