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CASE SERIES OF CHILDREN WITH MULTISYSTEM INFLAMMATORY SYNDROME ASSOCIATED WITH CORONARY ARTERY DILATATION

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ABSTRACT

Since the beginning of the severe SARS-CoV-2 pandemic, an increasing number of countries reported cases of a systemic hyperinflammatory condition defined as multi-system inflammatory syndrome in children (MIS-C). The clinical features of MIS-C can be an overlap of Kawasaki Disease (KD). We report on a cohort of 3 cases of children with SARS-coV2 related MIS-C presenting with clinical features compatible with Incomplete KD to the pediatric department over a period of 11 months from june 2021 to april 2022. In all the 3 cases, investigations showed persistently elevated inflammatory markers with leukocytosis and reactive thrombocytosis, serology showed positive for SARS-coV2 infection, 2d Echo showed coronary artery dilatation with Z score >+2. One case required ICU admission which was treated with IVIG, steroids and aspirin. One among the three cases was non responsive to treatment with steroids and aspirin needing increase in the dosages.

KEYWORDS: MIS-C, KD, IVIG.

INTRODUCTION

Since the beginning of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, an increasing number of countries reported cases of a systemic hyperinflammatory condition defined as multi-system inflammatory syndrome in children (MIS-C). This hyperinflammatory condition has also been termed as pediatric multisystem inflammatory syndrome (PIMS), pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIM-TS), pediatric hyperinflammatory syndrome, or pediatric hyperinflammatory shock. Initially published case series from different countries have common observations delineated from this MIS-C referred to overlapping clinical features of Kawasaki Disease (KD). While intravenous immunoglobulin (IVIG) is recommended as first line therapy and is successfully used in KD, some cases were responsive to treatment with steroids and aspirin. The 3 cases had MIS-C with positive serology for SARS-coV2 infection. We describe the clinical characteristics, laboratory data and treatment management which were observed and collected from these cases.

METHODOLOGY

Our clinical study is a case series that includes all eligible patients identified during the study registration period (consecutive, formal). It describes the experience on a small group of patients (observational, descriptive research design), contains demographic information about them and was conducted retrospectively.

Study Period

The present study was done over a period of 11 months from june 2021 to april 2022 at RRMCH, Bangalore, karnataka.

Inclusion Criteria

A. Fever for more than 3 days along with two of the following criteria of :
1. Muco-cutaneous inflammatory signs
2. Hypotension and shock
3. Coagulopathy
4. Elevated inflammatory markers
5. Evidence of more than 1 organ involvement

B. All patients with a positive serology for SARS-CoV2 or RTPCR positive.
C. Positive Echocardiographic findings.

Exclusion Criteria

1. Other obvious microbiological cause for inflammation including bacterial sepsis.

2. Patients with evidence of a hyperinflammatory state having negative serology for SARS-CoV2 and negative nasopharyngeal smear and
3. Without positive echocardiographic findings.

DISCUSSION

The COVID-19 outbreak has led to unique challenges in appropriate patient management. The disease, while primarily affecting the lungs, has a spectrum of presentations ranging from asymptomatic to viral pneumonia and respiratory failure, and in children, multisystem inflammatory syndrome in children (MIS-C). As our understanding of this condition continues to improve, its complex multisystem effects are being revealed.

Several pathophysiological mechanisms may underpin how severe COVID-19 disease may contribute to the development of dilated coronaries. The COVID-19 virus binds to the ACE2 receptor, which is expressed on cardiac myocytes and vascular endothelium. Furthermore, severe COVID disease is known to trigger a cytokine storm, with increased levels of IL1B, IFNγ, GCSF, MIP1A, and TNF. Finally, a stress response in relation to respiratory failure, hypoxia, and shock will trigger an increase in cortisol and catecholamines. The combination of all the above factors may precipitate the development of dilated coronaries.

Here we report a case series for which cases were selected based on inclusion and exclusion criteria, as all the cases presented with fever more than 3 days, Elevated inflammatory markers were present for all the three cases. In view of fever with leukocytosis and elevated inflammatory markers, broad spectrum antibiotics were given for which there was no response. Hence investigations were repeated which showed persistently elevated inflammatory markers with leukocytosis and thrombocytosis following which Tier 1 workup was done which excluded other microbiological causes for inflammation(like dengue, malaria, typhoid). One of the case presented with thrombocytopenia with leukocytosis and hypoalbuminemia, where as the other 2 cases presented with thrombocytosis, leukocytosis and hypoalbuminemia. All the 3 cases showed positive SARS-Cov2 serology.

All 3 patients presented with persistent fever above 39^{o} C for more than 5 days and were treated with broad spectrum antibiotics at admission, despite which there was no response. In all the 3 cases, investigations showed persistently elevated inflammatory markers with leukocytosis and reactive thrombocytosis, serology showed positive for SARS-coV2 infection, 2d Echo showed coronary artery dilatation with Z score >+2.

	Case 1	Case 2 b/o	Case 3
Clinical features			
Age in years/sex	3 years 3 months/ female	1 year 5 months/ Male	3 years
Comorbidities	No	No	No
Presenting symptoms			
Fever>3days, >40◦C	+	+	+
Abdominal pain	-	-	-
Diarrhea/Emesis	+	-	-
Rash	+	-	+
Conjunctival injection	+	-	+
lymphadenopathy	-	-	-
Extremity edema/erythema -	-	-	+
Headache/irritability	+	+	-
Mucosal inflammation	+	+	+
Respiratory insufficiency	-	-	-
Shock	-	-	-
Acute encephalopathy	-	-	-
Cardiopulmonary support			
Ventilation support	-	-	-
O2 support	-	-	-
Vasoactive-(support/diuretics/corticosteroids)	Methyl prednisolone given	Prednisolone given	Methyl prednisolone given
Maximal values in laboratory			
Platelets	18000	700000	
Albumin	2.1	2.8	
D dimer(mg/L)	3.92	0.83	52400
C-reactive protein (mg/L) (Ref: <10 mg/L)	+(12)	+(12)	2.4
Procalcitonin (mcg/l) (Ref: <2 mcg/l)	-	-	

Ferritin (mcg/L) (Ref: 14-101 mcg/L)	235	114.5	
Neutrophil count (%)	67%	50%	
N-Terminal pro-Brain natriuretic peptide -proBNP (ng/L) (Ref: 0-300pg/ml)	29881	-	
SARS-CoV-2 testing SARS-CoV-2 serology	+ve for IgG and IgM(>10)	+ve for IgG and IgM	+ve for IgG
I**maging**			
Coronary dilation (Z-score)	2.41	1.92	2.1
IVA aneurysm	-	-	-
Cardiac dysfunction	-	-	-
Cardiopulmonary imaging (US; X-ray; C/T scan)	Xray chest- normal	Xray chest- normal	Xray chest- normal
Cerebral imaging (MRI) Localized	-	-	-
Abdominal imaging (US; C/Tscanner)	HSM, mild ascites	Cystitis	-
Antibiotics (duration-days	Piptaz for 5 days	Ceftriaxone for 10days	Ceftriaxone for 7 days

CONCLUSION

Cardiac involvement is common in children with multisystem inflammatory syndrome associated with the Covid-19 pandemic. The majority of children have significantly raised levels of N-terminal pro B-type natriuretic peptide, ferritin, D-dimers, and cardiac troponin in addition to high C-reactive protein and procalcitonin levels.

This type of study is most useful for describing the potential effectiveness of new interventions and for describing the effectiveness of interventions on unusual diagnoses.

In conclusion, our case series reports on clinical and laboratory findings of MIS-C and incomplete KD and response to conventional treatment modalities.

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