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Case series

COVID-19 related multisystem inflammatory syndrome in children (MIS-C): A case series from Ethiopia

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Abstract

Background: *One in twenty of people affected by the ongoing COVID-19 pandemic have been children and adolescents. A unique complication in this age group is the Multi-inflammatory syndrome associated with COVID-19 (MIS-C). We report a single-center case series of children diagnosed with MIS-C from Addis Ababa, Ethiopia.*

Case descriptions: *This case series describes the clinical presentation and treatment outcomes of four male patients presenting at a mean age of 3 years and 11 months. All fulfilled the World Health Organization case definition criteria for the Multi-inflammatory syndrome associated with COVID-19. All were not eligible for vaccinations against severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) at the time of their diagnosis. They were treated with varying combinations of intravenous immunoglobulin, aspirin, and corticosteroids, and all recovered upon completion of their follow-up period.*

Conclusion*: Cases of Multi-inflammatory syndrome associated with COVID-19 are often misdiagnosed. This case series highlights when to consider such a diagnosis and its therapeutic options.*

Keywords*: MIS-C, Ethiopia, COVID, SARS-CoV-2, children*
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Introduction

The Multi-inflammatory syndrome associated with COVID-19 (MIS-C) is a post-infection hyper-inflammatory response primarily recognized among patients aged 18 years and less (1). It has an incidence of 316 persons per 1000000 SARS-CoV-2 infections in persons younger than 21 years (2). There is minimal data from African countries concerning severe COVID-19 infections and MIS-C among children. In a recently published retrospective cohort study from six African countries, suspected or confirmed MIS-C was diagnosed in 3.8% of children hospitalized with COVID-19 (3).

Following the reporting of the first child with MIS-C in Ethiopia in March 2021, there has been little data on further descriptions of children diagnosed with the syndrome in the country, barring a second case report in July 2022 (4,5). We report a single-center case series of four children diagnosed with MIS-C.

Case series

The parents of three children could recall their child coming into contact with a confirmed case of COVID-19 infection within the preceding 4 to 6 weeks. Their lab work-up revealed lymphopenia in one child, neutrophila and elevated creatinine in two children each and normal platelet counts, serum albumin, liver enzymes, coagulation profile, urinalysis and chest imaging in all four. Tests specific to their diagnosis and their management protocols are summarized in table 1.

None had a positive antigen or PCR test for SARS CoV-2. None of them had coronary artery dilatations or aneurysms in their echocardiography studies but two had acute mitral regurgitations and minimal pericardial effusion which resolved during follow-up studies at two and six weeks following discharge from hospital. All of them were having normal left ventricular systolic function as depicted

by normal ejection fraction and fractional shortening.

The mean duration of their hospital admission was 5.25 days. All were managed with intravenous immunoglobulin (IVIG) and aspirin and did not require admission to an intensive care unit. One child developed adverse reaction to the intravenous immunoglobulin with high grade fever, chills, rigor and his regimen was changed to a high dose (2 mg/kg/day) oral Prednisolone.

Table 1: Summary of the MIS-C specific diagnosis tests and treatment for all cases

Lab parameter	Case A	Case B	Case C	Case D
Age at presentation	4 yy 8 mo	2 yy 10 mo	4 yy 3 mo	3 yy 11 mo
Gender	Male	Male	Male	Male
Elevated C-reactive protein	Yes	Yes	Yes	Yes
Elevated SARS CoV-2 specific IgM and/or IgG	Yes (IgM and IgG)	Yes (IgG)	Yes (IgM)	Yes (IgG)
SARS CoV-2 PCR	Negative	Negative	Negative	Negative
SARS CoV-2 antigen test	Negative	Negative	Negative	Negative
Criteria met for Kawasaki disease	Yes (complete)	No	Yes (incomplete)	Yes (incomplete)
Echocardiographic abnormalities	Acute Mitral regurgitation	None	Acute Mitral regurgitation	None
Elevated troponin	Not done	Not done	Not done	Yes
Admission to intensive care unit	No	No	No	No
Vasoactive agents given	No	No	No	No
Corticosteroids given	No	No	No	Yes *
IVIG given	Yes	Yes	Yes	Yes
Aspirin given	Yes	Yes	Yes	Yes
Length of stay in hospital	5 days	2 days	10 days	4 days
Patient outcome	Improved	Improved	Improved	Improved

* Oral Prednisolone

Discussion

The diagnosis of the four cases we presented were made based on the WHO diagnostic recommendation for MIS-C for children and adolescents aged 18 years or less (6). These criteria are based on a fever of more than 3 days and two or more of suggestive dermatologic, cardiovascular or gastrointestinal features and coagulopathies. Gastrointestinal manifestations like diarrhea, abdominal pain, vomiting and mesenteric adenitis are the commonest features of MIS-C (7). This should be accompanied by elevated inflammatory markers (CRP, ESR etc), absence of alternative diagnoses, and evidence of COVID-19 infection (usually positive SARS-CoV-2 serology and a negative PCR and antigen test) or a likely contact with a patient with confirmed COVID-19.

Delayed or excess cytokine storm and an aberrant immune response mediated by non-neutralizing IgG antibodies are some of the contributing factors for MIS-C (8). The presentation of MIS-C may vary from mild disease (a less common outcome than in acute COVID-19) to features resembling Kawasaki disease with or without shock, toxic shock syndrome and macrophage activation syndrome (9). There is a slight male preponderance (55%) for MIS-C as reflected in our case series (7). A decreased systolic ventricular function is the commonest cardiologic abnormality with mild mitral regurgitation another well-described feature. Coronary aneurysms are uncommon in MIS-C (10,11). A raised CRP (94%), neutrophilia (83%) and lymphopenia are the commonest hematologic and inflammatory marker abnormalities as also evidenced in our case series (6). A recently published study has noted patients with MIS-C to be at a higher risk for coagulopathies among children and adolescents (12).

Intravenous immunoglobulin (2 g/kg over 12 hours) and aspirin with an initial anti-inflammatory dose of 30 to 50 mg/kg/day till afebrile and later a lower dose of 3 to 5 mg/kg/day for six weeks (if echocardiography is normal at follow-up at 6 weeks) or indefinitely (if coronary artery abnormalities are detected) can be used to treat children presenting with complete or incomplete Kawasaki disease (13). Alternative therapies include corticosteroids alone or intravenous immunoglobulin alone or a combination of the two (14,15).

In conclusion, we describe the multi-inflammatory syndrome associated with COVID-19 in four young

Ethiopian children. Further studies are needed to characterize this patient population and institute early recognition and therapy. As more cases are diagnosed, efforts for provision of treatment options like intravenous immunoglobulin at a wider scale in referral hospital should be emphasized.

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