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Case Series

Typical and Atypical Presentation of MIS-C in New York City Children; a Case Series

Jesus C Jaile IV*, Motoki Yasuda, David Mortel, Aracelis Fernandez, Sundari Periasamy, and Vicky Kuo

Department of Pediatrics, Harlem Hospital Center, Affiliate of Columbia University, New York, NY

***Corresponding author**

Jesus C Jaile IV, Department of Pediatrics, Harlem Hospital Center, Affiliate of Columbia University, New York, NY, USA, Email: jailej@nychhc.org

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Abstract

We present a case series centered around typical and atypical presentations of Multisystem inflammatory syndrome in children (MISC) residing in the NYC area. Preliminary research suggests that children are just as likely to become infected with SARS-CoV-2, but the presentations can be drastically different. This manuscript aims to highlight the different ways children can present with MIS-C, and the acute clinical course following presentation.

ABBREVIATIONS

MISC: Multisystem Inflammatory Syndrome in Children; PICU: Pediatric Intensive Care Unit; BPM: Beats per minute; ECG: Electrocardiogram; NYC: New York City

INTRODUCTION

The epidemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has had an exponential rise in cases worldwide. Originally thought of as a disease affecting the elderly population, and underdeveloped countries, Coronavirus-19 (Covid) quickly became a force in the United States, and the pediatric population, especially in the epi-center of the United States, New York City. In adults Covid-19is typically characterized by severe bilateral pneumonias, and respiratory failure, while the respiratory course in the pediatric population was thought to be more benign [1]. As we get to understand the disease course with passing time, it appears to be linked to a severe complication currently known as Multisystem Inflammatory Syndrome in Children (MIS-C). Currently in our population MIS-C is devoid of acute respiratory symptoms, and has predominantly presented with fevers and features similar to an acute gastroenteritis like illness.

The disease pathogenesis seems to be characterized by a cytokine storm and activation of the hosts innate immunity against its own tissues. Because of this pathology multiple organ systems are susceptible to the induced tissue damage seen in MIS-C (2). Notably the past few weeks there has been an increased incidence of Kawasaki like vasculitis and acute gastroenteritis, in patients who also meet the criteria for MIS-C. This case series serves to describe the demographics, presentation, clinical course, and outcomes of patients who met the criteria for MIS-C, and what steps were taken to manage them in the acute phase.

CASE SERIES

Case 1

A 6-year-old African American male, (Table 1) with past medical history of ADHD, presented with 3 day history of fever abdominal pain and mild diarrhea, but did not endorse any rash, headache, conjunctivitis or shortness of breath (Table 2). He was admitted to the pediatric floor with a diagnosis of dehydration, in the setting of gastroenteritis, and managed with IV fluids and observation. Nasopharyngeal SARS-COV-2 polymerase chain reaction (PCR), testing was negative on admission, but antibody testing returned positive (Table 1). On day of hospitalization (DOH 2), the fever spikes began to cluster more with a temperature max of 105.1 degrees Fahrenheit, and inflammatory markers up trended from admission (Table 3). Chest x-ray showed a retrocardiac shadow, consistent with possible pneumonia, and trace pleural effusion. He was commenced on antibiotic treatment for bandemia and presumed pneumonia with ceftriaxone at 50 mg/kg/day, and on DOH 3 developed shortness of breath, and hypotension, so antibiotics were switched to vancomycin, and an echocardiogram was ordered. Echocardiogram showed depressed systolic function (46%), with pleural effusion. In the setting of his echocardiogram findings, increasing BNP (Table 3), and worsening clinical status he was transferred to a cardiac pediatric intensive care unit (PICU), for step up care. During his PICU stay he received antibiotics for 72 hours with the fevers

resolving on day of illness (DOI) 6. He received pressor support in the form of dobutamine, and milrinone, for 48 hours. Respiratory support was required with Bi-level positive airway pressure (Bi-PAP), for 48 hours and a 5 day steroid course of Prednisolone 2 mg/kg/day. On DOH 4 his D-dimer peaked at 19,000 and he was started on heparin 50 mg/day for prophylaxis. At the time of discharge he was stable on room air, afebrile, with a follow up echocardiogram showing normal systolic heart function (Table 4).

Case 2

A 2 week old African-American male, with Newborn Screen positive for sickle cell trait, was admitted to the pediatric floor for rule out sepsis in the setting of positive Covid IgG antibodies (Table 1). He was born at 35 weeks gestation and received 48 hours of Ampicillin and Gentamycin after birth for rule out sepsis due to being in utero with a fetal demise twin. Also pertinent to prenatal history was that his mother was PCR positive for Covid-19 on routine screening 24 hours prior to delivery. He was discharged home on day of life (DOL) 7, after negative blood cultures and no fevers. One week following his discharge from the Neonatal Intensive Care Unit (NICU) he returned to the emergency department febrile with a max temperature of 101.9, and poor feeding. Initial emergency department workup was significant for dehydration, but negative for any elevations in inflammatory markers (Table 3). Lumbar puncture was performed which came back with no organism growth, and normal cellular counts. During his hospitalization he had multiple runs of tachyarrhythmia, over 200 BPM, but the remainder of the cardiac workup, including echo, four limb blood pressures and EKG came back within normal limits. His fevers peaked at 102.4 degrees on DOI 3 and were completely gone by DOI 5 and he was discharged on DOI 6. During his stay he remained stable on room air, and did not require any oxygen support, or respiratory medications (Table 4).

Case 3

A 12-year-old Hispanic female, who was Covid IgG positive (Table 1), was admitted to the pediatric floor for management of presumed appendicitis. She presented to the emergency department with 4 days of fever, right lower quadrant pain, vomiting and diarrhea, with initial CT scan findings of acute appendicitis, with an exuberant amount of surround inflammation (Figure 1). She was placed on Piperacillin with Tazobactam (Zosyn) and managed as if she would be taken to the operating room (OR), for appendectomy. Prior to reaching the OR her pre-operative labs were concerning for unproportionable inflammation and systemic illness. Her floor course was complicated by increasing inflammatory markers, leukocytosis, worsening acidosis, large volume diarrhea, and hypotension (Table 3). On hospital day 2 the patient was noted to have hypotension and a new onset 2/6 systolic murmur. The hypotension was managed with normal saline bolus 20 cc/kg with good response. EKG was done revealing low voltage QRS complex, so the decision was made to transfer to a cardiac care unit. Upon transfer echocardiogram showed mildly decreased systolic function (49%), but no signs of aneurysm or effusion. Inflammatory markers continued to trend up, reaching their peak on day of hospitalization 3, which was also the last day of fevers in this child. Due to up trending coagulation markers (Table 3), she was started on Lovenox 0.5 mg/kg twice a day for thrombosis prophylaxis. She completed a 7 day course of Zosyn, with resolution of her abdominal pain, diarrhea, inflammatory markers and fevers. Ultrasound prior to discharge showed resolved inflammation of the bowel, and no signs of acute appendicitis with normalization of lab values.

Table 1: Table showing the demographics of the patients in our case series. Included is age, race, sex, comorbidities, BMI, and PCR / Antibody status.

SUBJECT	1	2	3	4
AGE	6 Years	2 Weeks	10 Months	19 Months
SEX	Male	Male	Female	Female
RACE	Black	Black	Black	Black
CO-MORBIDS	ADHD	Sickle Cell Trait	Ex-Premie (26 wk)	None
BMI	17	15.6	13.5	14.2
Sars-Cov-2 PCR	Negative	Negative	Negative	Negative
COVID IgG	Positive	Positive	Negative	Positive

Table 2: Table showing the presenting complaints (PC) and symptoms that arose during hospitalization in the patients within our case series.

SUBJECT	1	2	3	4
Fever	Yes PC	Yes PC	Yes PC	Yes PC
Rash	No	No	No	Yes PC
Diarrhea	Yes PC	No	Yes	No
Abdominal Pain	Yes PC	N/a	N/a	No
Conjunctivitis	No	No	No	Yes
Respiratory Distress	Yes	No	No	No
Shock	Yes	No	No	No
Tachycardia	Yes	Yes	Yes	Yes

Table 3: Table showing the initial labs values, the peak lab values, and the discharge lab values of commonly followed MISC labs.

	Case 1			Case 2			Case 3			Case 4		
	Admission	Peak	Discharge	Admission	Peak	Discharge	Admission	Peak	Discharge	Admission	Peak	Discharge
CBC (4.0-11)	8.6	12	7.7	10.3	14.6	8.3	16	19	5.7	10.19	8	6.95
HCO3 (18-24)	18	12	22	18	17	20	18	14	23	19	17	21
BNP (<450)	1776	18,056	60	654	2132	1311	32	172	22	293	1495	58
Troponin (<.01)	<.01	<.01	<.01	<.01	<.01	<.01	<.01	<.01	<.01	<.01	<.01	<.01
D-Dimer (<.5 ug/mL)	1.1	>20,000	0.34	0.29	0.71	0.24	3	15.9	6.7	7.8	8.7	0.61
Ferritin (7-14 ng/mL)	560	580	102	120	140	120	135	268	166	65	175	114
Bands (0)	32	67	2	0	1	0	2	6	1	3	6	1
Pro-Calcitonin (<.1 ng/mL)	13.9	20.9	0.1	0.17	0.29	0.12	2.5	2.5	0.3	0.17	0.39	0.11
LDH (135-214 u/L)	431	475	325	N/A	N/A	N/A	160	160	159	367	367	301
Fibrinogen (<5.0 mg/dL)	310	475	225	N/A	N/A	N/A	566	913	548	441	496	479
CRP (<5.0 mg/dL)	184	352	3.2	<.1	<.1	<.1	118	325	0.6	14	17.9	3.5
Blood Culture	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative
Lactate (0.2 - 1.6 mmHg)	3.4	5.3	1.2	N/A	1	1	1.3	1.9	0.4	N/A	N/A	N/A
ESR (0-10 mm/Hr)	N/A	N/A	N/A	N/A	N/A	N/A	92	129	66	N/A	N/A	N/A

Table 4: Table summarizing length of stay (LOS), treatment modalities, and outcomes of the cases.

SUBJECT	1	2	3	4
LOS	8 Days	6 Days	9 Days	4 Days
Outcome	PICU / Home	Floor / Home	PICU / Home	Floor / Home
Resp. Support	Bi-Pap	None	High Flow	None
Prednisolone	Yes	None	Yes	None
IVIG	None	None	None	None
Antibiotics	Rocephin + Vancomycin	Rocephin + Acyclovir	Zoysn	Rocephin
Heparin	Yes	None	Yes	Yes

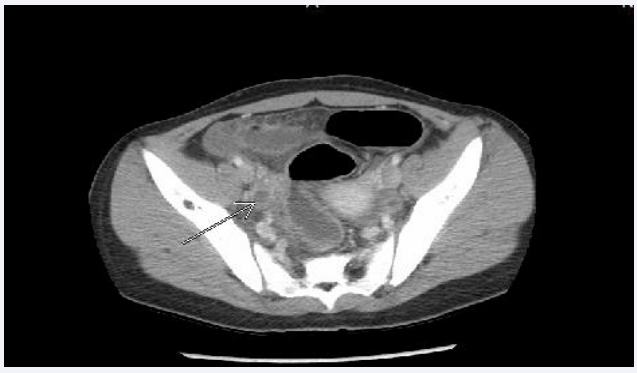

Figure 1 CT scan image showing initial evidence of Acute appendicitis described in case 3.

Case 4

A 19-month-old African American female, with no significant past medical history, admitted to the PICU for management of desquamation of the hands and feet in the setting of a febrile illness, with positive Covid IgG antibody (Table 1). Presented to the emergency department with 2 days of fever, temperature max of 103.6, and one day of respiratory distress in the form of tachypnea not associated with wheezing or desaturations (Table 2). While in the emergency department she was noted to have desquamation of her hands and feet (Figure 1A-C), and history of subjective conjunctivitis, and was admitted secondary to these findings. On admission inflammatory and coagulation markers were mildly elevated (Table 3), and during admission peaked on day of hospitalization 2, requiring treatment with ceftriaxone 50 mg/kg/day and Lovenox 0.5 mg/kg daily as prophylaxis. Due to the concern for Kawasaki disease and increasing in cardiac markers an echocardiogram was obtained, showing no abnormalities, including no coronary artery aneurysms. Due to the unremarkable cardiac findings IVIG therapy was not initiated, and patient was managed on ceftriaxone and prednisolone Blood cultures and respiratory viral panels were collected and noted to be negative.

DISCUSSION

The emergence of SARS-COV-2 stemming from the COVID-19 pandemic is an ongoing global crisis, with long-term implications for the world of medicine. At the beginning of the pandemic one of the unique features of the disease was the relatively low incidence among pediatric patients, and the even lower incidence of systemic disease in the pediatric age group [2]. However as the virus evolved and more data became available it became apparent

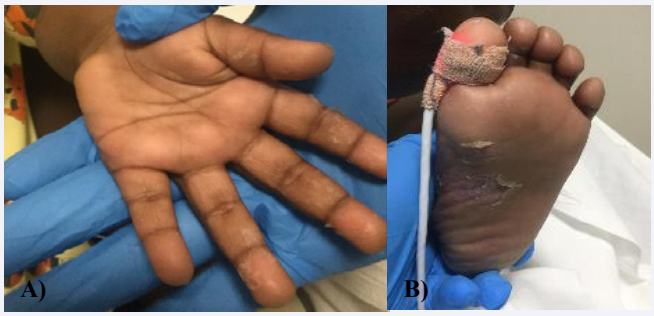

Figure 2 A-B: Desquamating rash described in case.

that children were being affected by a disease sequalae, known as MIS-C, highlighted by persistent fever, diarrhea, variable rash and severe illness including myocardial dysfunction [3,4].

The findings described in this case series further supports the sequalae of SARS-COV-2 as a multisystemic illness ranging from mild to severe in the pediatric population. Unlike the adult population, there is a wider range of presenting symptoms providers must be aware of in order to not overlook a potentially fatal complication. MIS-C was first described as a Kawasaki like illness, with some aspects similar to those of Kawasaki disease, including: prolonged fever, multisystem inflammation with skin rash, lymphadenopathy, diarrhea, meningism, and high levels of inflammatory biomarkers. None of the patients in our series had aneurysm on echocardiogram, and intravenous immunoglobulin (IVIG), was not used to treat any of our subjects, even though it has become a popular treatment option in some centers. A number of adjunct therapies have been used because of the profound inflammatory response and KD-like features, with intravenous immunoglobulin (IVIG), corticosteroids, anakinra (an interleukin-1 receptor antagonist), and tocilizumab (an anti-interleukin-6 receptor monoclonal antibody) being most often reported. Many centers have treated children that present most similar to KD with traditional therapy used for KD. The authors of this study recommend giving IVIG 2 g/kg and aspirin 20–25 mg/kg/dose every 6 h (80–100 mg/kg/day), for all patients with KD-like illness, evidence of excessive inflammation (ferritin >700 ng/mL, CRP >30 g/dL, or multisystem organ failure), or cardiac involvement [5].

Systolic ventricular dysfunction was the main cardiac feature in this series, with none of the patients having sings of aneurysm. Myocardial inflammation can be documented in a high proportion of patients with Kawasaki disease, and it usually precedes coronary artery abnormalities. In Kawasaki disease, myocardial edema is the main finding without ischemic damage and with limited cell necrosis as evidenced by the mild to moderate elevation of troponin I [6]. None of our patients had elevations in troponin, suggesting that the cardiac dysfunction caused by MISC is less necrotic in nature than the dysfunction in Kawasaki disease. The high levels of BNP in our series suggest a mechanism of myocardial edema or stunning, as the primary cause of the dysfunction. Left ventricular systolic dysfunction improved rapidly in our patients, as it does in Kawasaki disease, concomitant with a decline in the inflammatory process.

MIS-C can also present with signs and symptoms that mimic those of septic shock and toxic shock syndrome. In any patient who presents with severe multisystem involvement, it is recommended they should receive prompt empiric broad-spectrum antibiotic therapy. An appropriate empiric regimen consists of ceftriaxone with escalation to vancomycin if the patient deteriorates further. Ceftaroline plus piperacillin-tazobactam is an alternative regimen, particularly for children with acute kidney injury. Clindamycin is added if there are features consistent with toxin-mediated illness (eg, erythroderma). Antibiotics should be discontinued once bacterial infection has been excluded if the child's clinical status has stabilized. The mainstay of treatment in our case subjects was oral steroids in the form of Prednisolone 2 mg/kg/day and antibiotics, which is consistent with the general acceptable treatment guidelines for this rapidly evolving disease process.

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