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Teaching Case Report

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A case of multisystem inflammatory syndrome in children (MIS-C) mimicking Kawasaki disease

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Abstract

Introduction: Severe acute respiratory syndrome coronavirus-2 infection has emerged as a multisystem disorder during the pandemic of C*oronavirus* disease of 2019 (Covid-19). Multisystem inflammatory syndrome of children (MIS-C) is a rare grave complication of Covid-19 due to immunodysregulation.

Case Presentation: We present a 14-year-old boy who had fever, cardiac and gastrointestinal symptoms, mucocutaneous manifestations and cervical adenopathy with a background of recent asymptomatic Covid-19 infection. Inflammatory and cardiac biomarker panels were raised in the absence of other microbial causes of inflammation.

Discussion: Although there were overlapping features of Kawasaki disease, the ultimate diagnosis was MIS-C. He was successfully managed with immunomodulatory therapy.

Keywords: Covid-19, MIS-C, Kawasaki disease, immunodysregulation, methylprednisolone

INTRODUCTION

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV 2) infection has emerged as a multisystem disease with an adult predilection. [1] Infection among children was considered a milder disease. [2, 3] Subsequently, a hyper-inflammatory syndrome resembling Kawasaki disease (KD) began to coexist in children infected with SARS-CoV 2. [4] This new disease entity was coined as a multisystem inflammatory syndrome of children (MIS-C).

CASE REPORT

A 14-year-old boy presented with fever, watery diarrhoea, and intermittent chest pain for 6 days. He had a contact history of Covid-19 three weeks ago. His Rapid antigen test for SARS-CoV 2

(RAT) was positive 17 days ago. He has been asymptomatic for 11 days until he developed fever. He was febrile with bilateral conjunctival suffusion and erythematous lips. There was no maculopapular skin rash or periungual desquamation. He had bilateral tender multiple discrete anterior cervical lymphadenopathies. There was no hepatosplenomegaly. The respiratory rate was 40 cycles per minute. Lungs were clear on auscultation. Oxygen saturation was 98% on room air. Pulse rate and blood pressure were 105 beats per minute and 114/65 mmHg

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respectively. Gallop rhythm and murmurs were not present.

Full blood count revealed neutrophil leukocytosis with lymphopenia and mild thrombocytopenia with a normal haemoglobin. C-reactive protein and erythrocyte sedimentation and procalcitonin was raised. Urine and stool analysis were normal. Blood, urine and stool cultures were negative. Tests for dengue and leptospirosis were also negative. Cardiac Troponin I was elevated. Serum lactate dehydrogenase, ferritin, D-dimers and N-terminal pro brain natriuretic polypeptide (NT-proBNP) level were raised. Triglyceride level was elevated while serum fibrinogen level was within normal limits. He had transaminitis and hypoalbuminemia. Coagulation and renal functions were normal (Table 01). An electrocardiogram did not show any evidence of myocarditis. Chest radiograph revealed a cardiomegaly although there was no perihilar congestion or pleural effusion. (Figure 01) Transthoracic echocardiogram (TTE) was normal with an ejection fraction of 60%. There was no detectable coronary artery dilatation.

Table 01 Summary of blood investigations

Laboratory tests	Results	Reference range
Total white cell count (/L)	12.5 x 10^9	4-10 x 10^9
Absolute neutrophil count (/L)	12 x 10^9	2-7 x 10^9
Absolute lymphocyte count (/L)	0.42 x 10^9	1-3 x 10^9
Hemoglobin (g/L)	12.2	12-15
Platelet count (/L)	117 x 10^9	150-450 x 10^9
C-reactive protein (mg/L)	340	<3
Erythrocyte sedimentation rate (mm 1st hour)	115	<7
Procalcitonin (ng/mL)	72.6	<0.05
Cardiac Troponin I (ng/mL)	21469	<14
Lactate dehydrogenase (U/L)	461	150-250
Ferritin (µg/L)	576	30-400
D-dimers (ng/mL)	1285	<0.2
NT-proBNP (pg/mL)	994	<125
Triglyceride (mg/dL)	430	<150
Fibrinogen (g/L)	3.4	203-382
Alanine transaminase (IU/L)	65	<45
Aspartate transaminase (IU/L)	144	<32
Serum albumin (g/dL)	2.9	35-52

Throughout the hospital stay patient didn't require supplemental oxygen or inotropic support. With elevated cardiac biomarkers, possibility of a viral or bacterial myocarditis was considered as a differential diagnosis. But patient fulfilled the case definition for MIS-C according to World Health Organization (WHO) criteria. He was treated with intravenous immunoglobulin (IVIG) and IV methylprednisolone (IVMP) for 5 days. Oral aspirin and subcutaneous low molecular weight heparin were commenced. Treatment response was monitored with serial cardiac and inflammatory biomarkers which normalized during the course of illness. Patient was discharged on day 8 of hospital stay with oral prednisolone and aspirin with the plan of reviewing in 2 weeks for a cardiac assessment.

DISCUSSION

MIS-C manifests 4 to 8 weeks after Covid-19 infection. Pathophysiology is postulated to be due to immune dysregulation. Spike protein of SARS-CoV 2 acts as a super antigen which activates the innate immune system leading to a surge of proinflammatory cytokines. [5] Common clinical features include fever, diarrhoea, abdominal pain, maculopapular skin rash and shock. Less common features include conjunctivitis, cervical adenopathy and skin desquamation. [6] KD predominantly affects children less than 5 years of

age. But MIS-C is a disease of young children and adolescents. [7] KD can be diagnosed when 4 out of 5 principal criteria are met along with fever for 5 or more days. Principal criteria include oedema and desquamation of extremities, polymorphous rash, conjunctival injection, erythema and cracking of lips or strawberry tongue and unilateral cervical lymphadenopathy. When lesser than 4 criteria are fulfilled, KD can still be diagnosed if there are coronary artery anomalies. Additional criteria include anemia, leukocytosis, thrombocytosis, hypoalbuminemia, pyuria and raised CRP and ALT. [8] Our patient had fever with conjunctival injection, erythematous lips and bilateral cervical adenopathy with raised inflammatory markers and mild hypoalbuminemia. But there were no demonstrable coronary artery anomalies, thrombocytosis or pyuria. Therefore, diagnosis of KD was unlikely. After 17 days from RAT positivity, cytokine storm was unlikely. According to WHO case definition for MIS-C, our patient fulfilled 3 out of 5 main criteria including mucocutaneous manifestation, evidence of myocardial dysfunction and acute gastrointestinal problems. (Table 02) Hence, our patient was diagnosed as a case of MIS-C.

Management of MIS-C includes immunomodulatory agents such as IVIG and IVMP [9, 10] Standard dose of IVIG is 2 g/kg single dose. IVMP can be started at a low to moderate dose (1-2 mg/kg/day) in mild MIS-C, although severe or refractory cases warrant higher doses (10-30 mg/kg). Duration of IVMP should be 5-7 days followed by oral prednisolone 1 mg/kg/day. Low dose aspirin (3-5 mg/kg/daily) is recommended for at least 4 weeks. Patients should have cardiac reassessments in 2nd and 6th week with a TTE. Steroids should be tailed off gradually.

In conclusion, MIS-C is a rare serious complication of Covid-19. It has a significant overlap with KD. Early commencement of immunomodulatory agents has a mortality benefit.

Table 02 WHO case definition of MIS-C

Children and adolescents 0–19 years of age with fever ≥ 3 days
AND
Two of the following main criteria 1. Rash or bilateral non-purulent conjunctivitis or mucocutaneous inflammation signs 2. Hypotension or shock 3. Features of myocardial dysfunction, pericarditis, valvulitis or coronary abnormalities (echocardiographic findings or elevated Troponin/NT-proBNP) 4. Evidence of coagulopathy 5. Acute gastrointestinal problems
AND
Elevated markers of inflammation (ESR, CRP or procalcitonin)
AND
No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes.
AND
Evidence of COVID-19 **infection** or likely contact with patients with COVID-19.

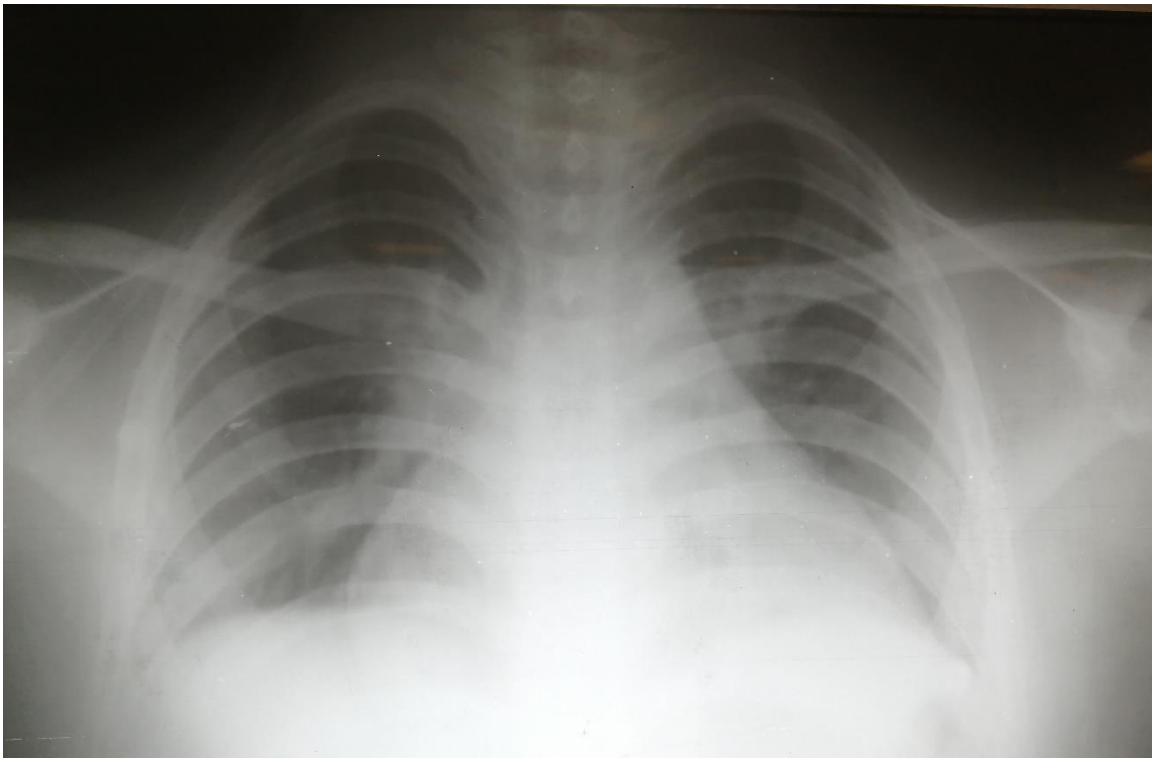

Figure 01: Chest radiograph showing cardiomegaly

Author declaration

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Author Contributions

All authors were involved in the management of the patient. Rathnayake M did the literature review and wrote the draft. Dassanayake L also contributed to the literature review. Fernando EAC and Sadikeen A did the final corrections before submission. All authors have read and approved the final manuscript.

Conflicts of interest

Authors declare no conflict of interest

Financial support

Not applicable

Ethics approval and consent to participate

Informed written consent was obtained from the patient and the father for publication of this case report.

Statement on Data availability

All necessary data and material are provided

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