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Case Report

Unresolved coronary artery aneurysms in an adolescent with multisystemic inflammatory syndrome in children associated with SARS-CoV-2 infection- what happens in the long term: a case report

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ABSTRACT

MIS-C, a well-known association with SARS-CoV-2 infection, has been a topic of significant interest. It presents with Kawasaki-like illness along with coronary artery dilation or aneurysms. In this report, we describe a particularly intriguing case of an adolescent with MIS-C presenting with coronary artery aneurysms persisting at the end of a 6-month follow-up, underscoring the importance of this condition. An 11-years-old adolescent female presented with fever, livedoid vasculitis rash over lower limbs, abdominal pain and breathlessness. Diagnosis of MIS-C was established based on the clinical findings, elevated inflammatory markers and positive SARS-CoV-2 IgG antibodies. Echocardiogram evidenced myocardial dysfunction with moderate pericardial effusion and coronary aneurysm. She was treated with intravenous immunoglobulins, steroids and aspirin. Serial follow-up until 6 months showed persisting skin changes and coronary aneurysms with normalized inflammatory markers. MIS-C and its related long-term outcome have been well recognized; however, longer follow-up is not just essential, but urgent in understanding this known yet novel condition.

Keywords: Coronary artery aneurysm, Case report, Long-term outcome, MIS-C

INTRODUCTION

MIS-C has been known to be associated with varied cardiac manifestations.[1] Incidence of MIS-C has decreased significantly since 2022, potentially because of widespread immunity to SARS-CoV-2 or it could be that newer variants are not virulent enough to cause MIS-C.[2] Previously, data was scarce to understand the long-term outcome of those children affected with MIS-C.

Recent studies have shown that most of them have good clinical outcomes with no residual sequelae when treated during the early phase of the illness. However, it is now evident that a tiny percentage go on to have residual disease when followed up. We describe an adolescent with MIS-C complicated by coronary aneurysms which largely remained unresolved at the end of 6 months, thus highlighting the need to closely follow up with these individuals who might be at risk of developing myocardial ischemia, thrombus or coronary stenosis that might occur in their adulthood similar to Kawasaki disease.[3]

CASE REPORT

An 11 years old female adolescent who was previously well presented with a 2 weeks history of discrete rashes involving bilateral lower limbs. She had high-grade fever spikes lasting for 3 days, diffuse abdominal pain and breathlessness lasting for one day prior to her presentation.

On examination, she was pale with elevated jugular venous pressure and bilateral pedal oedema. The skin had periungual desquamation and discrete non-blanching purpuric rashes distributed over both lower limbs

extending below the knees up to bilateral feet. (Figure 1A, B) She was febrile and tachycardic, her blood pressure was normotensive.

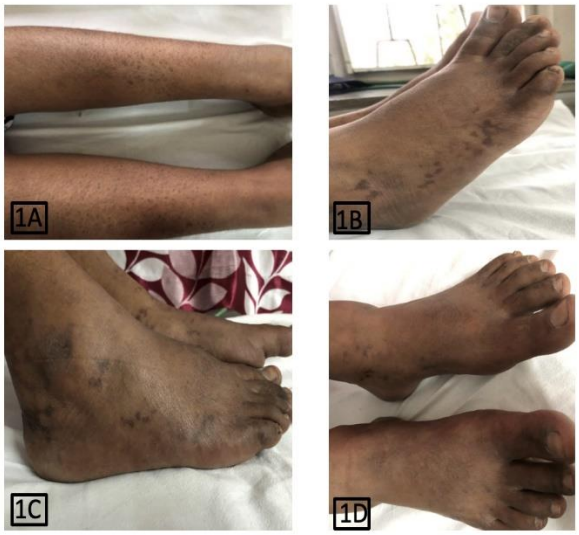

Figure 1: (1A and 1B) Livedoid vasculitis rash involving the anterior aspect of lower limbs and both feet. (1C and 1D) Follow up at the end of 6 months showing persisting rash.

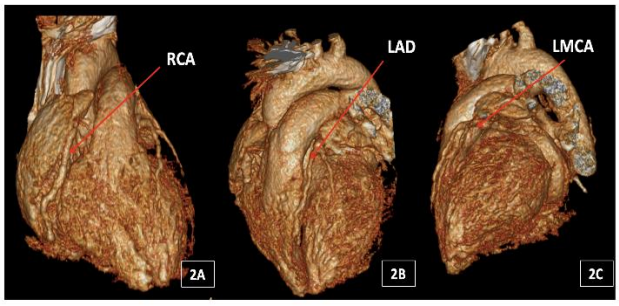

Figure 2: Cardiac computed tomography performed at the end of 6 months showing moderate aneurysm of RCA with a Z-score of 6.01 (2A), LAD with a Z-score of 8.82 (2B) and LMCA with a Z-score of 7.1 (2C).

Systemic examination revealed bilateral lung basal crepitation, hyperdynamic precordium and ejection systolic murmur of grade 3/6 over the pulmonary area with muffled heart sounds and hepatomegaly with no signs of ascites. Neurological examination was unremarkable. There was a history of contact with a SARS-CoV-2-positive family member weeks prior to the onset of her symptoms.

Baseline investigations (Table 1) performed showed anaemia, with neutrophilic leukocytosis and thrombocytosis. Inflammatory markers were raised. As our index child met the WHO criteria for MIS-C temporally associated with SARS-CoV-2, was further evaluated. RT-PCR was negative. SARS-CoV-2 immunoglobulin G antibodies were positive, confirming the same.[4] An echocardiogram performed at baseline showed moderate coronary aneurysms in LMCA, LCX, LAD and RCA arteries (Table 1).

She was treated with IVIG at a dose of 2 grams/kilogram along with intravenous methylprednisolone at 2 milligrams/kilogram/day for a total duration of 5 days. She was then switched to oral prednisolone at 1.5 milligrams/kilogram, which was gradually tapered and stopped in 6 weeks as per WHO guidelines.[5] Given presence of coronary aneurysms, she was also started on oral aspirin at an anti-platelet dose. Biologics such as IL-1 blocker Anakinra were considered but could not be accessed due to financial constraints. She gradually showed defervescence and clinically improved with declining inflammatory markers; hence, she was discharged.

On follow-up with serial echocardiograms at various intervals, it was noted to have unresolved coronary aneurysms at the end of 6 months, even though her inflammatory markers had normalised. (Table 2) Skin rash persisted as well. (Figure 1C, 1D) CT coronary angiogram performed at the end of 6 months revealed moderate aneurysm of RCA with a z-score of 6.01, LAD with a z-score of 8.82, LMCA with a z-score of 7.1 and no coronary stenosis. (Figure 2) She was advised to continue on oral aspirin and monitor closely but unfortunately lost to follow-up.

Table 1: Laboratory results of the index case at the time of presentation and serial echocardiographic findings at follow up.

Laboratory parameters	Values	Normal range
Haemoglobin	7.3 g/dl	11-16g/dl
Total leucocyte count	14420 cells/µl	4–10 ^ 3/ul
Neutrophils	11536 cells/µl	2–710 ^ 3/ul
Lymphocytes	2739 cells/µl	0.8–4.0 10 ^ 3/ul
Platelets	584000 cells/µl	150–450 10 ^ 3/ul
CRP	6.20 mg/dl	<1mg/dl
ESR	51 mm/1hour	0-10 mm/1hour
Serum creatinine	0.58 mg/dl	0.6-1.2 mg/dl
Serum sodium	133 mEq/l	135–145 mEq/l

Continued.

Laboratory parameters	Values	Normal range
Serum potassium	4.2 mEq/l	3.5–5.0 mEq/l
Serum chloride	102 mEq/l	90-110 mEq/l
PT	13 seconds	9-12 seconds
APTT	28 seconds	21-29 seconds
INR	1.08	0.9-1.2
D-dimer	1915 ng/ml	<500 ng/ml
Serum ferritin	587 ng/ml	Upto 150 ng/ml
MIS-C IgG antibodies	Positive	
Chest X-ray	Cardiomegaly	
Echocardiogram	Situs solitus, levocardia, left ventricle dilated, Mild Left ventricular dysfunction, aneurysms of LMCA, LCX, LAD and RCA arteries. Ejection fraction-50%, Fractional shortening-25%. Moderate pericardial effusion (Right atrium side=12 mm)	

Table 2: Serial Echocardiographic parameters performed at various intervals.

Timeline	EF (%)	LVD	PE	LMCA	LCX	LAD	RCA
Admission	50%	Mild	Moderate	5.7mm (Z-score: 5.79)	4mm (Z-score:3.43)	4.8mm (Z-score:5.78)	5.8mm (Z-score:6.39)
6 weeks	55%	Mild	Absent	5.3mm (Z-score:4.92)	3.7mm (Z-score:2.84)	5.2mm (Z-score:6.73)	5.8mm (Z-score:6.39)
3 months	49%	Mild	Absent	6.4mm (Z-score:7.31)	3.9mm (Z-score:3.22)	6.17mm (Z-score:9.01)	5.7mm (Z-score:6.18)
6 months	47%	Mild	Absent	6.4mm (Z-score: 7.1)	3.9mm (Z-score:3.09)	6.17mm (Z-score:8.82)	5.7mm (Z-score:6.01)

DISCUSSION

MIS-C after exposure to SARS-CoV-2 infection was known to be a rare manifestation in children during the pandemic.[6] One of the initial cases from India was reported in 2020.[7] MIS-C has now been well known to have substantial cardiovascular implications in the pediatric age group, even though majority have a mild form of illness which resolves without residual sequelae.[8] The most common cardiovascular manifestations noted were myocardial dysfunction, arrhythmias, pericardial effusion and coronary artery dilatation with reduced left ventricular ejection fraction.[1] Coronary artery dilation is usually mild or moderately sized, comprising 6% to 24% of the cases.[9]

During the initial phase of this emerging condition, individual cases were reported with a paucity of long-term outcome data. More data on long-term outcomes have recently reiterated the importance of close monitoring. A meta-analysis by Arantes et al, showed that coronary dilation or aneurysm was seen in 15.2% of the MISC cases worldwide and 9.3% had long-lasting manifestations.[10] A study from India by Priyankar et al, presented signal centre data alone involving 71 children with MIS-C, among which 26.8% had coronary artery aneurysms with Z-scores <5 and all of them normalised over 6 months of follow-up.[11] Sofia et al, reported 3 cases with giant aneurysms in MIS-C, among whom was a 12-years-old adolescent presenting with RCA, LAD giant aneurysms, which persisted even at the end of 6 months but had an improving trend and remains well on aspirin and warfarin.[9] Wacker et al, reported a 10-years-old with medium LAD and small RCA aneurysms in the context of MIS-C after treatment was followed up to 6 months with near normalisation of the coronary arteries, unlike our index case who persisted in having a residual aneurysm.[6] Chakraborty et al, in the long-term follow-up study of 80 children with MIS-C, had 17.5% coronary artery abnormalities and one had a persistent giant aneurysm at the end of 1 year.[12]

Metanalysis by Yasuhara et al, revealed that coronary artery abnormalities, including dilatation and aneurysms, were seen in 23.7% of the children at the baseline and persisted in 4.7% at 3 months and 5.2% at the end of 6 months.[13] Overall, it is evident that most of the cardiac complications of children with MIS-C resolve within months. However, studies have shown that a small proportion of them continue to have residual sequelae and need close follow up on long term.

CONCLUSION

MIS-C, once an emerging syndrome, has now become a well-known entity with coronary artery abnormalities in the form of dilatation or aneurysms as one of the recognised complications. Majority of them show resolution with early therapy. However, a smaller percentage can continue to have residual sequelae on long-term follow-up. MIS-C and its related long-term complications have only been recognised recently; hence,

close follow-up is vital in understanding these children's outcomes in adulthood.

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