Giant Coronary Aneurysms in an Infant: Dilemma of MIS-C

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Case Report

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Abstract

COVID-19 related MIS-C (Multisystem inflammatory syndrome in children) can present with cardiovascular complications like shock, arrhythmias, pericardial effusion, and coronary artery dilatation. The majority of MIS-C associated coronary artery abnormalities are dilation or small aneurysms which are transient and resolve in a few weeks[1, 2]. We present here a case of a 3-month-old child who was noted to have giant aneurysms of her coronary arteries (LAD and RCA) twenty-six days after testing positive for COVID-19. She was treated with IVIG, infliximab, and glucocorticoids along with aspirin, clopidogrel and enoxaparin. She did not show any signs of coronary ischemia or cardiac dysfunction but continued to have persistent giant coronary artery aneurysms involving the LAD (z-score ~35) and RCA (z-score ~30) [Fig. 1]. This study emphasizes the importance of early detection and aggressive management of MIS-C to prevent potentially life-threatening consequences.

Introduction

While acute COVID-19 infection typically causes mild or no symptoms in the pediatric population, reports from the United Kingdom and Italy surfaced in April 2020 describing an inflammatory syndrome associated with COVID-19 that caused a more severe illness in children now known as multisystem inflammatory syndrome in children (MIS-C). Ever since, a wide range of symptoms and clinical findings associated with MIS-C have been reported, including three different phenotypic subtypes—MIS-C without overlap with Kawasaki disease (KD) or acute COVID-19, MIS-C overlapping with KD, and MIS-C overlapping with severe acute COVID-19[3]. Based on similarities in patient presentations, MIS-C treatment has been largely dictated by standard KD treatment, including aspirin, IVIG, and glucocorticoids. However, limited reports have described a subset of MIS-C patients who experienced development or further progression of coronary aneurysms despite receiving current standard therapy[4], as observed in the patient presented in this case study.

Case Presentation

A 3-month-old female with no significant past medical history presented to the ED for 1 day of fever, cough, and increased fussiness. Her mother had a positive COVID-19 test several days prior, and the patient's other siblings were also ill. The patient's COVID-19 nasopharyngeal swab was positive, and she was sent home in stable condition. About 1 week later, the patient had several ED visits for recurrent fever, fussiness, diffuse rash which appeared on day 9, diarrhea, and decreased oral intake. She was also noted to have red, dry cracked lips and mild conjunctival erythema on exam. She was admitted to the hospital on day 11 of illness for further care of suspected acute COVID-19 infection. She was started on a 10-day course of dexamethasone 0.15 mg/kg/day. At that time, she had a normal BNP and troponin. An echocardiogram showed normal coronary arteries size, trace pericardial effusion, and normal systolic function. She was discharged home on day 15 and completed the 10-day course of dexamethasone.

On day 24 she was brought back to the ED for continued intermittent fevers, fussiness, recurrent rash, vomiting, diarrhea, and newly developed periorbital edema. She required supplemental oxygen briefly and was admitted to the pediatric intensive care unit (PICU) with persistent tachycardia. She was noted to be COVID-19, rhinovirus, and coronavirus OC43 positive. Her procalcitonin (0.66 ng/mL), CRP (27.8 mg/dL), D-dimer (2.75 ug/mL FEU), and platelets (794 K/uL) were elevated, and she was anemic (Hgb 8.0 g/dL). Her BNP was 162 pg/mL (Ref: Normal < 100 pg/ml), but her troponin was within normal limits. An echocardiogram (Fig. 2) obtained on day 26 revealed giant aneurysms of the right coronary (Z-score 24.43), left anterior descending (Z-score 27.17), and left circumflex, which was also confirmed with a CT angiogram. Treatment with 1 dose each of IVIG 2g/kg and infliximab 5 mg/kg was initiated along with aspirin 20.25 mg daily, clopidogrel 0.2mg/kg/day, and enoxaparin 1.5 mg/kg BID. During her admission she was also treated with captopril 0.05 mg/kg TID for blood pressure control. She was discharged home on day 33 with triple therapy (aspirin, clopidogrel and enoxaparin) and prednisolone which was tapered. She underwent cardiac catheterization at 9 months of age (Fig. 3) for persistent giant aneurysms of the coronary arteries. She remained clinically stable with no sign of thrombosis of her coronary arteries on dual antiplatelet therapy and enoxaparin. At the time of this report the patient is 6 months into the disease with stable giant coronary aneurysms (Fig. 1).

Discussion

Shock, cardiac arrhythmias, pericardial effusion, and coronary artery dilatation have been reported as acute cardiovascular complications of MIS-C. The majority of MIS-C associated coronary artery abnormalities are dilation or small aneurysms. There have only been a limited number of reported cases of giant coronary artery aneurysms as seen in this patient[1, 2]. In a study of 503 MIS-C patients who received echocardiograms, 13% of patients had coronary artery aneurysms and among those 79.1% normalized within 30 days and 100% by 90 days based on available data[5]. However, several other studies have reported persistence or even progression of coronary artery aneurysms after discharge, Hejazi et al [6] described at least one patient whose medium coronary artery aneurysm persisted at 6 months of follow up[7, 8]. While MIS-C is widely accepted as a post-infectious inflammatory disorder, the exact mechanism causing aneurysms in the setting of MIS-C is unclear. Some have hypothesized that similar to Kawasaki disease (KD), inflammatory cytokines in circulation disrupt the arterial wall. As coronary abnormalities seen in MIS-C are generally relatively mild and resolve rapidly[9, 10], some have also speculated that coronary enlargement is a result of proinflammatory vasodilation instead. Based on the shared clinical features with KD, current treatment for MIS-C includes aspirin and IVIG with the addition of glucocorticoids for moderate to severe illness or inadequate response to IVIG. Infliximab, a tumor necrosis factor antagonist, has also been associated with improvement of coronary artery aneurysms in MIS-C patients with severe illness or who failed to respond to IVIG[7].

Our patient initially presented with symptoms that aligned more closely with acute COVID-19 infection, but by the time of her first hospital admission she met WHO and CDC criteria for MIS-C as well as criteria for incomplete KD. Her case was unusual in that there were no labs or imaging suggesting cardiac involvement on her first admission other than negligible pericardial effusions, yet by her second hospital

admission she had developed giant coronary artery aneurysms. IVIG is thought to prevent coronary artery aneurysm formation and progression in KD[8]. Despite standard therapy with aspirin, IVIG, glucocorticoids, and infliximab, this patient's aneurysms progressed for 5 more days before stabilizing and have not regressed since discharge. Coronary artery aneurysm progression after IVIG seen in this patient and others underlines the importance of learning more about the difference in pathophysiology between KD and MIS-C so that potentially better directed therapies can be developed[4]. Her case also raises the question of whether closer outpatient follow up or earlier treatment could have prevented such significant aneurysms or affected the probability of regression.

Conclusion

This patient's case highlights the difficult task facing clinicians in treating MIS-C patients who may present with innumerable combinations of symptoms, clinical findings, and disease courses. Therefore, further research which identifies patient characteristics or biomarkers associated with coronary artery aneurysm formation will be highly useful. Physicians would also benefit from further research on which MIS-C patients are at greatest risk of coronary artery aneurysms refractory to standard treatment as well as potential alternative treatment pathways for these patients. In the meantime, patients with presentations suspicious for MIS-C should receive close outpatient follow up for cardiac complications. In this manner, patients such as the subject of this case study may avoid cardiac outcomes secondary to MIS-C with potentially life-threatening consequences.

Declarations

I. **Ethical approval:** Consent obtained from legal guardian of minor patient. All information is anonymous. IRB approval not required

II. **Funding details:** No funding was secured for this case report.

III. **Conflict of interest:** All the authors have no conflicts of interest to disclose.

IV. **Informed Consent:** Obtained from legal guardian of minor patient. All information is anonymous.

V. **Authorship contributions:**

AD wrote manuscript.

KW edited manuscript, figures and references.

SH edited manuscript and figures.

AG wrote and edited manuscript, figures and references.

All authors reviewed the manuscript.

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Figures

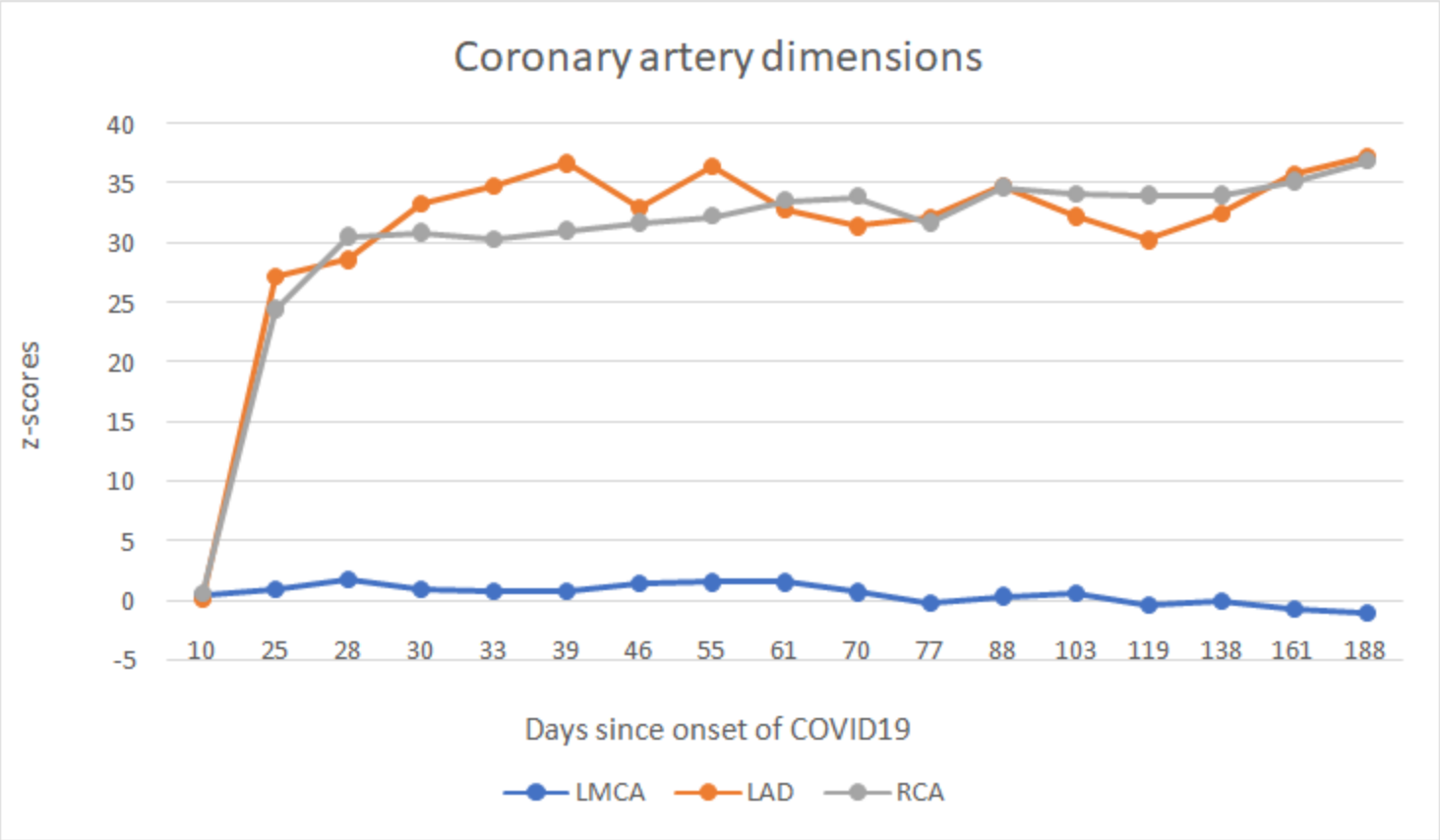


Figure 1

Coronary arteries *z* scores versus time through the course of disease.

LMCA: Left main coronary artery; LAD: Left anterior descending artery; *RCA*: Right coronary artery

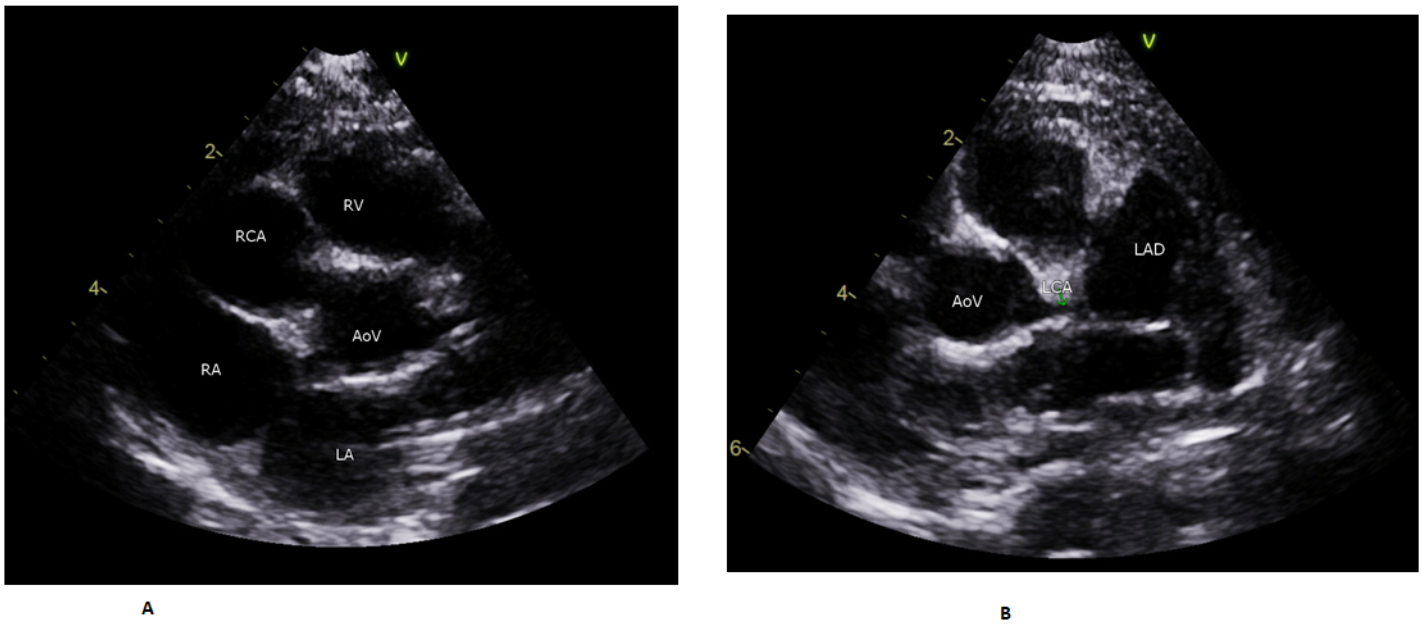
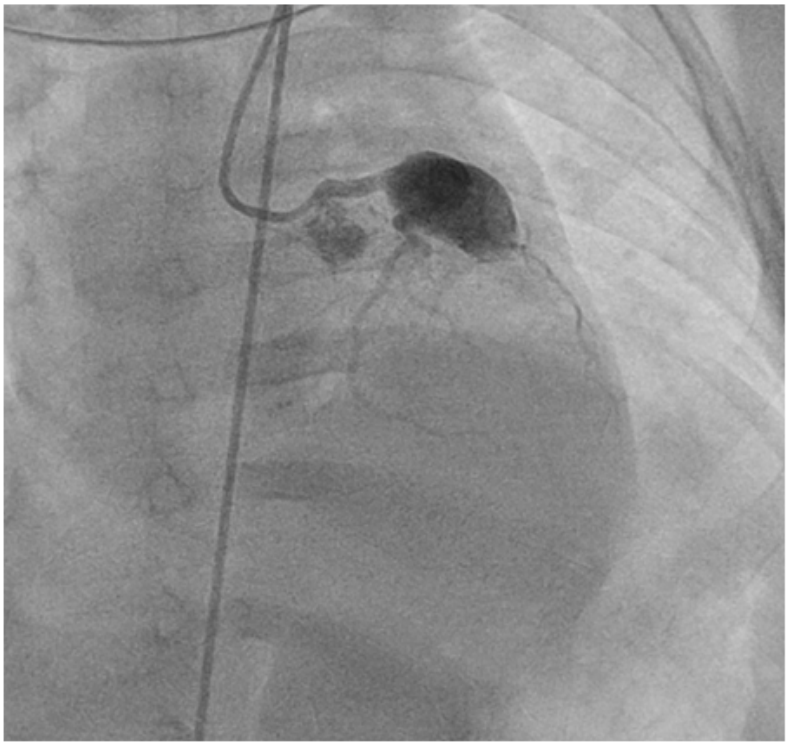


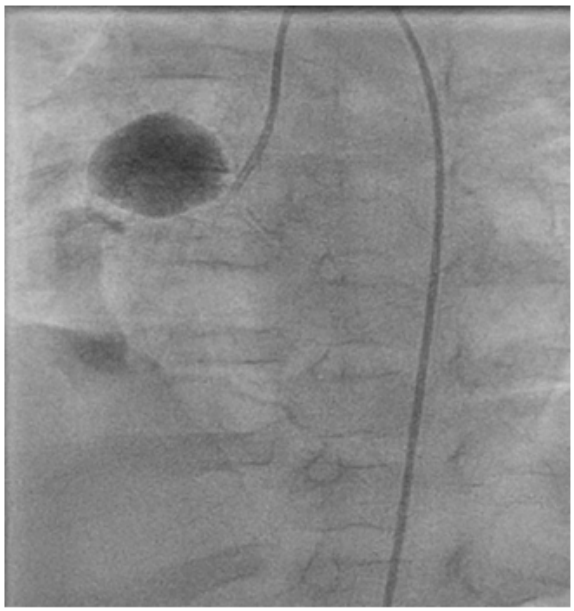
Figure 2

2D TTE, basal parasternal short axis images showing giant aneurysms of A) RCA (12.9 mm; z-score 36.8), B) LAD (10 mm, z-score 37.2) and normal LMCA (1.6 mm, z-score -1)

LMCA: Left main coronary artery; LAD: Left anterior descending artery; *RCA*: Right coronary artery



A



B

Figure 3

Angiographic images of coronary arteries demonstrating

A. Giant aneurysm of the LAD, normal dimensions of the LMCA and distal segments

B. Giant saccular aneurysms of proximal and mid-portions of the RCA

LMCA: Left main coronary artery; LAD: Left anterior descending artery; *RCA*: Right coronary artery