Title

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CASE REPORT

INTERMEDIATE

CLINICAL CASE

Coronary Sinus Thrombosis and Post-Myocardial Infarction Syndrome in Kawasaki Disease

Rare Causes of Pericardial Effusion

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ABSTRACT

The hypercoagulable state in Kawasaki disease (KD) may lead to complex cardiovascular sequelae. We present the case of a 2-month-old infant with complete KD complicated by giant coronary artery aneurysms, coronary sinus thrombosis, and post-myocardial infarction syndrome (Dressler syndrome), resulting in 2 distinct episodes of pericardial effusion. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2023;26:102077) © 2023 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 66-day-old non-Hispanic white boy presented with 3 days of fever and 1 day of rash associated with vomiting, poor feeding, lethargy, and fussiness. Physical findings included generalized macular rash, red lips, and inguinal erythema.

PAST MEDICAL HISTORY

The infant was born at full term via normal vaginal delivery to nonconsanguineous parents, with no significant perinatal issues, past medical or surgical history except for an uneventful circumcision at 1 month of age. His height, weight, and occipital-frontal circumference were tracking normally, and his vaccinations were up-to-date before the presenting illness.

LEARNING OBJECTIVES

- To appreciate the hypercoagulable state and noncoronary cardiovascular complications in Kawasaki disease.
- To understand various potential causes of pericardial effusion in Kawasaki disease.

DIFFERENTIAL DIAGNOSIS

Differential diagnoses included infectious causes such as viral exanthem, Kawasaki disease (KD), and less common autoinflammatory disorders.

INVESTIGATIONS

Initial evaluation did not identify a source of infection, including negative bacterial culture of urine, blood, and cerebrospinal fluid, polymerase chain reaction of respiratory viral panel on nasopharyngeal specimen, and stool rotavirus antigen. An atraumatic

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ABBREVIATIONS AND ACRONYMS

CAA = coronary artery aneurysm

CRP = C-reactive protein

ECG = electrocardiogram

IV = intravenous

KD = Kawasaki disease

LAD = left anterior descending coronary artery

LCx = left circumflex coronary artery

MI = myocardial infarction

RCA = right coronary artery

lumbar puncture showed mild cerebrospinal fluid pleocytosis (red blood cells: 30/μL, total nucleated cells: 11/μL with 13% neutrophils, 12% lymphocytes, and 71% monocytes) with normal glucose and protein concentrations. Evidence of systemic inflammation included elevated C-reactive protein (CRP) (24.5 mg/dL) and erythrocyte sedimentation rate (81 mm/h), thrombocytosis (485 × 10^3/mL), normocytic anemia (hemoglobin: 7.2 g/dL, age-adjusted *z*-score: −4.1) and hypoalbuminemia (2.6 g/dL). The white blood cell count was 5.0 × 10^3/mL with 8% neutrophils, 54% lymphocytes, 3% atypical lymphocytes, and increased bands (13%), metamyelocytes (5%), and monocytes (13%). Hepatobiliary enzymes and troponin I levels were normal.

An echocardiogram showed aneurysms of the left main coronary (2.57 mm, body surface area-adjusted *z*-score: +3.4 using the Dallaire method[1]), left anterior descending coronary (LAD) (3.28 mm, *z*-score: +7.15), and proximal right coronary (RCA) (2.60 mm, *z*-score: +4.14) arteries with no pericardial effusion. The initial electrocardiogram (ECG) was unremarkable.

MANAGEMENT

The infant was admitted to a local children's hospital and empirically treated with intravenous (IV) ceftriaxone and vancomycin. He then developed conjunctival injection and extremity swelling, and a diagnosis of Kawasaki disease was made. He received IV immunoglobulin on day 4 of fever, and 1 dose of infliximab (10 mg/kg) on day 5 because of coronary artery aneurysms (CAAs).[2] He was also started on aspirin (55 mg/kg/d) with clopidogrel added on day 6. On day 7, IV methylprednisolone (2 mg/kg/d) was initiated due to persistent fever. Although his fever abated thereafter, coronary artery diameters worsened on repeated echocardiographic studies by report.

On day 17, the infant developed a small circumferential pericardial effusion, which progressed to a large (21.2 mm) effusion over 5 days with right atrial compression. He was transferred to pediatric intensive care unit, where he received anakinra for persistently elevated CRP, and IV heparin infusion in view of worsening CAAs starting on day 20. Periungual desquamation of multiple toes was documented on the same day. On day 22, he underwent

FIGURE 1 Day 23 Electrocardiogram Showing Myocardial Infarction

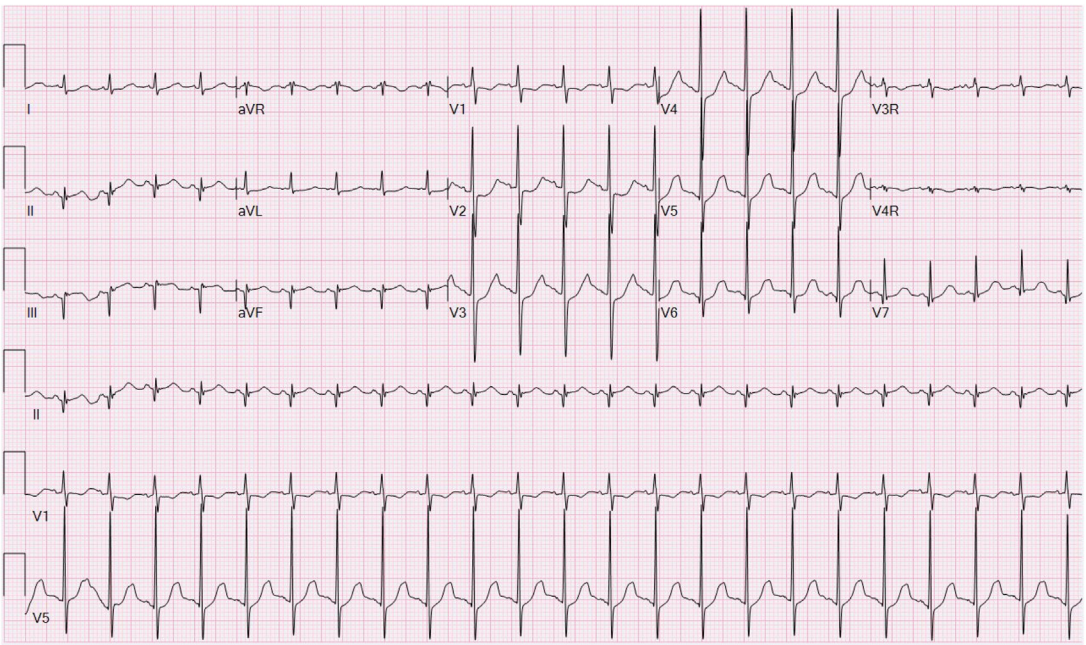
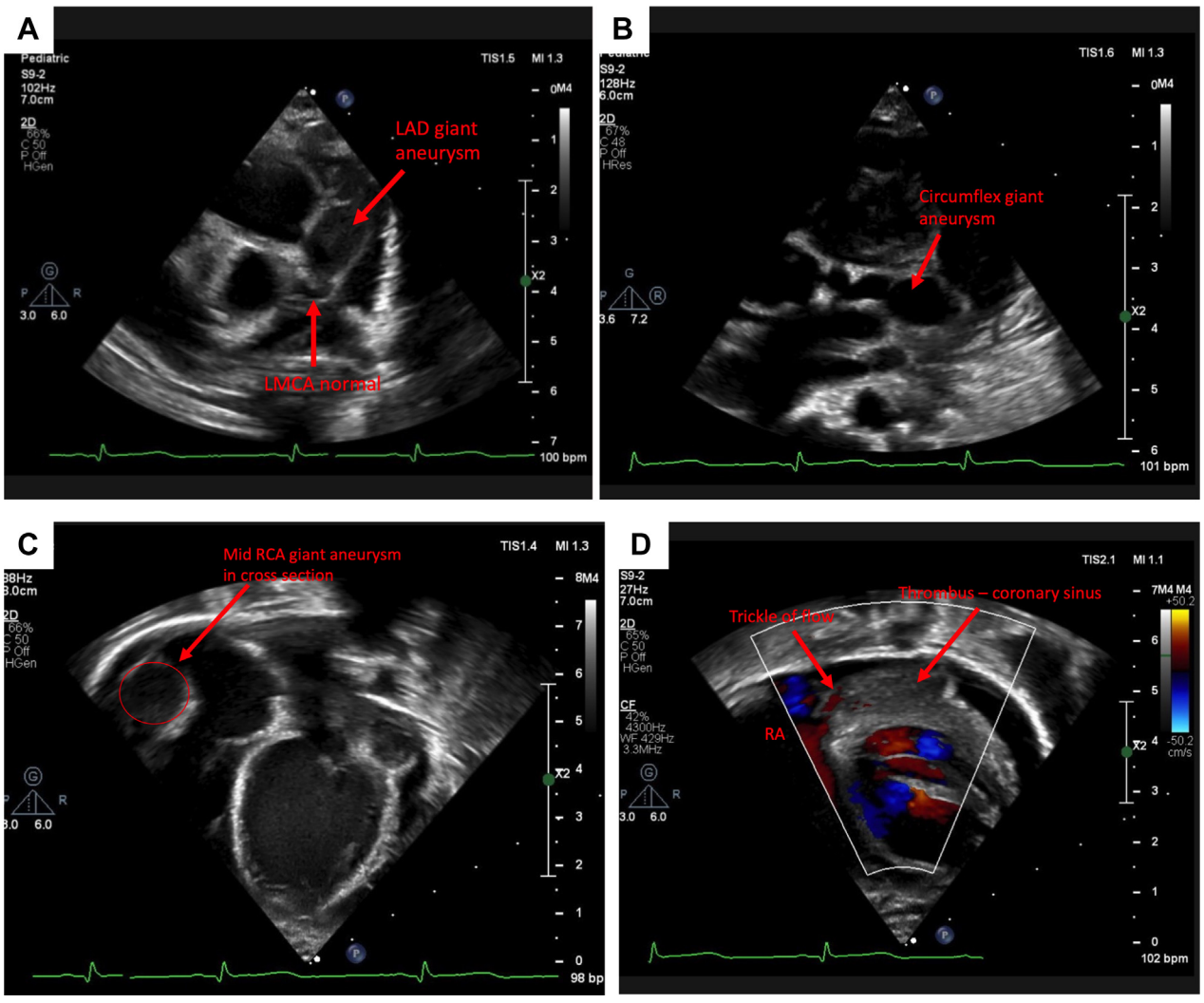


FIGURE 2 **Day 23 Transthoracic Echocardiogram Showing Diffuse Giant CAAs**



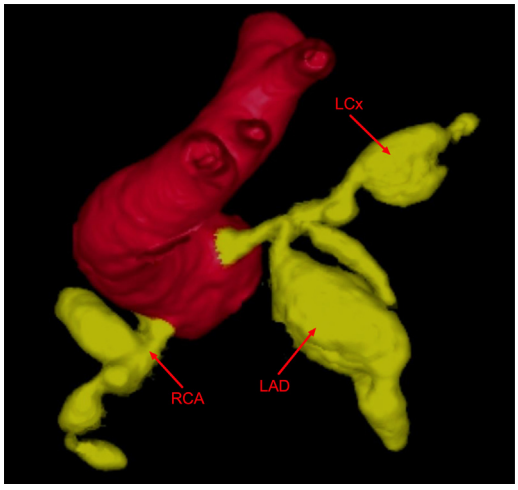
(A and B) Parasternal short-axis view; (C and D) 4-chamber view with posterior angulation assessing coronary sinus in D. CAA = coronary artery aneurysm; LAD = left anterior descending artery; LMCA = left main coronary artery; RA = right atrium; RCA = right coronary artery.

pericardiocentesis with placement of pericardial drain, which produced 75 mL of sterile transudative fluid. Cyclosporine was also started for additional immunomodulation.

On day 23, the infant was transferred to our center. On arrival, myocardial infarction (MI) was suggested by inferior ST-segment elevation with lateral depression on ECG (**Figure 1**) and elevated troponin-I that peaked 1 day later (8.35 ng/mL). An echocardiogram showed wall motion abnormality and multiple fusiform CAAs involving LAD (*z*-score: +24.3), left circumflex coronary artery (LCx) (*z*-score: +38.7), proximal (*z*-score: +8.4) and mid-RCA (*z*-score: +33.0) (**Figures 2A to 2C**, Videos 1 to 3). The LCx and coronary sinus were completely occluded by thrombus (**Figure 2D**, Video 4), which was confirmed by cardiac computed tomography (**Figure 3**). Despite these abnormalities, the left ventricular ejection fraction remained 50% to 55% (bullet formula). He was treated with nitroglycerin and 3 days of thrombolytic therapy with tissue plasminogen activator, heparin, and bivalirudin,[3] which re-established some flow through the thrombi.

The pericardial drain was removed on day 27 of illness after many days without output, and his steroid and cyclosporine doses were tapered off. Other

FIGURE 3 3-Dimensional Reconstruction of Coronary Arteries From Day 24 Cardiac Computed Tomography Showing Giant Aneurysms



LCx = left circumflex coronary artery; other abbreviations as in Figure 2.

medications included propranolol, spironolactone, and captopril for compromised myocardial function from ischemic injury. His CRP normalized on day 30 of illness.

On day 36 of illness, he developed poor feeding and lethargy with a new increase in CRP level (10.8 mg/dL from 0.7 mg/dL). Moderate pericardial effusion was demonstrated on a repeat echocardiogram. He was treated for post-MI syndrome, also known as Dressler syndrome, with colchicine that was later changed to anakinra due to gastrointestinal intolerance. Pericardial effusion resolved by day 50 of illness, and the infant was discharged 3 days later with persistent giant aneurysms in the LAD, mid-RCA, and LCx, on captopril, carvedilol, dual antiplatelet therapy (aspirin and clopidogrel), and enoxaparin.

DISCUSSION

KD is the leading cause of acquired pediatric cardiovascular disease in developed countries.[4] Although CAAs are the major concern,[4] other cardiovascular complications are less common. The mechanism of coronary sinus thrombosis is proposed to involve endothelial damage, hypercoagulability, and venous stasis, the key components of Virchow's triad.[5] Coronary sinus thrombosis as a cause of large pericardial effusion has not been reported in KD.

The 2 episodes of pericardial effusion in this infant were likely due to different causes. Although small pericardial effusion is common in the acute phase as an echocardiographic feature suggestive of KD,[6] massive pericardial effusion in the subacute phase was not typical. Coronary sinus thrombosis was the top suspect, which causes increased transcapillary pressure and direct myocardial injury from venous engorgement.[7] Coincident with the re-establishment of flow through the coronary sinus thrombus, the pericardial effusion resolved. By contrast, the second episode occurred 2 weeks after an MI and was coupled with a rising CRP, consistent with post-MI syndrome.[8]

Post-MI, or Dressler syndrome, is a rare occurrence in infants, principally due to the low incidence of MI in this age group. Because the condition is understudied in pediatric patients, its treatment relies on evidence from adults, including non-steroidal anti-inflammatory drugs, colchicine and steroids.[9] The limited pediatric experience poses significant challenges in treating infants and children with different physiology and clinical profile, such as possibly poorer tolerance to side effects seen in this baby. In view of the success of IL-1 blockade with rilonacept in recurrent pericarditis among patients who were 12 years and older,[10] we used an IL-1 receptor antagonist, anakinra, and observed good clinical response.

FOLLOW-UP

The infant was followed 1 week later in our KD clinic. A repeat ECG and echocardiogram demonstrated no new changes, and the laboratory tests showed normal cardiac biomarker levels and improving thrombocytosis. He returned home and had close follow-up with the local pediatric cardiologist.

Three months after discharge, both a follow-up echocardiogram and a repeat computed tomography angiogram showed resolution of the coronary sinus thrombosis, but giant CAAs persisted in all 3 vessels. The reported left ventricular ejection fraction was 53% by M-mode.

CONCLUSIONS

We present a 3-month-old male infant with KD complicated by giant CAAs, coronary sinus thrombosis, and post-MI syndrome that resulted in 2 distinct episodes of pericardial effusion. This case highlights the hypercoagulable state and extracoronary cardiovascular complications in KD as potential causes of pericardial effusion in the subacute stage of this disease.

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REFERENCES

1. Dallaire F, Dahdah N. New equations and a critical appraisal of coronary artery Z scores in healthy children. *J Am Soc Echocardiogr*. 2011;24(1):60–74.

2. Miyata K, Bainto EV, Sun X, et al. Infliximab for intensification of primary therapy for patients with Kawasaki disease and coronary artery aneurysms at diagnosis. *Arch Dis Child*. 2023;108(10):833–838. https://doi.org/10.1136/archdischild-2023-325639

3. Burns JC, El-Said H, Tremoulet AH, et al. Management of myocardial infarction in children with giant coronary artery aneurysms after Kawasaki disease. *J Pediatr*. 2020;221:230–234.

4. Newburger JW, Takahashi M, Burns JC. Kawasaki disease. *J Am Coll Cardiol*. 2016;67(14):1738–1749.

5. Masood W, Sitammagari KK. Coronary sinus thrombosis. In: *StatPearls. Treasure Island, FL*. StatPearls Publishing; 2022.

6. McCrindle BW, Rowley AH, Newburger JW, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a scientific statement for health professionals from the American Heart Association. *Circulation*. 2017;135(17):e927–e999.

7. Stewart RH, Rohn DA, Allen SJ, Laine GA. Basic determinants of epicardial transudation. *Am J Physiol*. 1997;273(3 Pt 2):H1408–H1414.

8. Khan AH. The postcardiac injury syndromes. *Clin Cardiol*. 1992;15(2):67–72.

9. Adler Y, Charron P, Imazio M, et al. 2015 ESC guidelines for the diagnosis and management of pericardial diseases: the Task Force for the Diagnosis and Management of Pericardial Diseases of the European Society of Cardiology (ESC). *Eur Heart J*. 2015;36(42):2921–2964.

10. Klein AL, Imazio M, Paolini JF. Phase 3 trial of interleukin-1 trap rilonacept in recurrent pericarditis. reply. *N Engl J Med*. 2021;384(15):1475–1476.

KEY WORDS coronary sinus thrombosis, Dressler syndrome, Kawasaki disease, pericardial effusion, post-myocardial infarction syndrome

APPENDIX For supplemental videos, please see the online version of this paper.