

## Various coronary artery complications of Kawasaki disease: Series of 5 cases and review of literature

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### ABSTRACT

Kawasaki disease is a generalized systemic vasculitis of unknown etiology involving medium and small size blood vessels throughout the body, virtually always involving the coronaries. In many part of this world, it is more common than rheumatic fever and viral myocarditis. Here, we are reporting 5 cases with history suggestive of Kawasaki disease in the early life, presenting with different coronary artery abnormalities. One of the patients had left main coronary artery cut-off, and the remaining 4 had some form of coronary artery aneurysms. 3 patients were given medical management, 1 patient had coronary bypass grafting, and the remaining 1 was planned for surgical correction. All the patients were stable on subsequent follow-ups.

**Key words:** Aneurysm, coronary complication, India, Kawasaki disease

### INTRODUCTION

Kawasaki disease is a generalized vasculitis of unknown etiology. In 1967, Tomisaku Kawasaki described this illness, also termed “mucocutaneous lymph node syndrome”, which had been affecting infants and young children in Japan.<sup>[1]</sup> Most cases occur between the ages of 6 months and 8 years. Diagnosis requires fever and 4 out of 5 principal clinical features (conjunctivitis; erythematous lips, oral cavity; palms and soles; polymorphous exanthema of the body trunk; swelling of the cervical lymph nodes) or if fewer than 4, patients should also have documented coronary artery disease diagnosed by echocardiography or coronary

angiography.<sup>[2]</sup> Cardiac, particularly coronary artery complications are well-known fact in this syndrome. Here, we are reporting 5 cases [Table 1] with past history of Kawasaki disease presenting with coronary artery abnormalities.

### CASE REPORTS

#### Case 1

7-year-old boy with documented history of Kawasaki disease at the age of 1 year, treated conservatively without using intra-venous immunoglobulin (IVIG), presented to us with shortness of breath (NYHA class 3). Echocardiography revealed feature suggestive of dilated cardiomyopathy with left ventricular ejection fraction (LVEF) of 30%. Angiogram [Figure 1] revealed normal right coronary artery (RCA) and left main coronary artery (LMCA) cut-off at mid part with collateral filling from right coronary. Further evaluation by cardiac stress testing revealed presence of provokable ischemia. After stabilization of heart failure,

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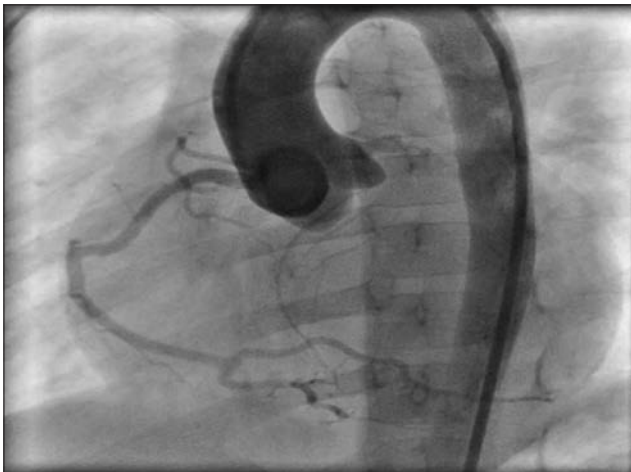
he was referred to cardiothoracic surgery for coronary artery bypass grafting (CABG).

### Case 2

11-year-old boy with history of Kawasaki disease at 3 years of age treated without any IVIG presented with non-specific chest discomfort. Echocardiogram showed ostial dilatation of RCA with normal ventricular function. Coronary angiography revealed aneurysm of proximal RCA with internal diameter of 9.2 mm [Figure 2a]. He was started with aspirin 5 mg/kg body weight and warfarin keeping INR between 2 to 2.5. On more than 1 year follow-up, he is doing fine with these medicines.

### Case 3

15-year-old boy presented with exertional chest



**Figure 1:** Non selective coronary angiogram showing normal RCA and LMCA cut-off from mid part with collateral filling from right system

discomfort and occasional palpitation. He had a history of Kawasaki disease at the age of 1.5 years. His baseline ECG and 24 hour holter monitoring was within normal limits. Echocardiogram detected dilatation of LMCA with preserved LVEF. Coronary angiogram revealed giant aneurysm of LMCA with maximum diameter of 12 mm [Figure 2b]. He was similarly put on oral aspirin and anti-coagulation therapy and keeping well on 6 months follow-up.

### Case 4

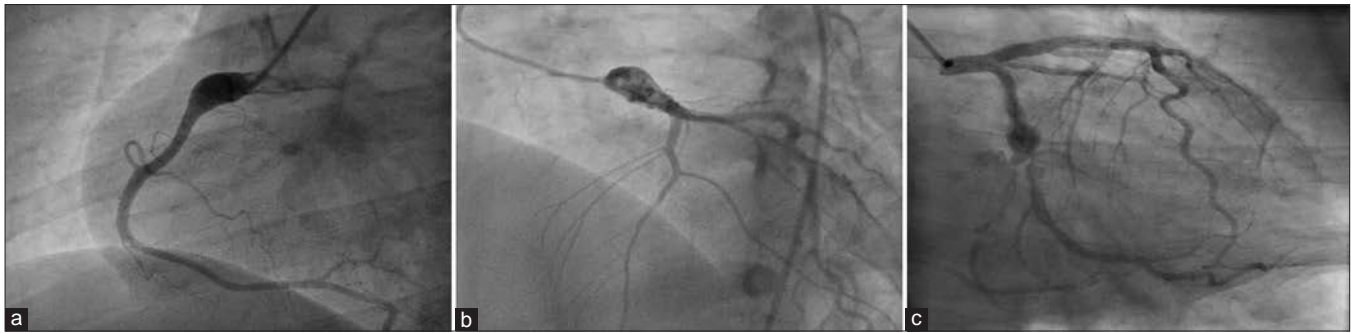
19-year-old male presented to us with exertional chest pain and dyspnea for last 6 months. He had a history of fever for 3 weeks-duration at the age of 4 years associated with conjunctival redness and skin rash over trunk. Echocardiogram revealed left ventricular posterolateral wall hypokinesia with LVEF of 46%. Coronary angiography showed aneurysm of left circumflex (LCX) artery with maximum internal diameter measuring 8.8 mm, followed by severe stenosis of LCX and 1<sup>st</sup> obtuse marginal branch [Figure 2c]. Though no documents were available, his childhood exanthem was postulated to be Kawasaki disease. On dobutamine stress echo, he was detected to have viability in LCX territory. He was kept on oral anti-coagulation, aspirin, and enalapril along with other anti-anginal medications and later referred for surgical correction in the form of aneurysm closure and bypass grafting to coronaries distal to stenosis.

### Case 5

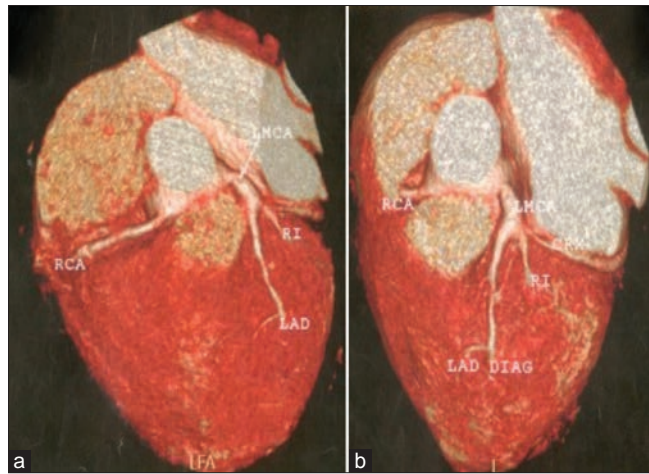
6-year-old boy with history of Kawasaki disease at the age of 3 years was complaining of occasional chest tightness.

**Table 1: Summary of clinical findings of the 5 cases of Kawasaki disease**

	Case 1	Case 2	Case 3	Case 4	Case 5
Age (years) at presentation	7	11	15	19	6
Age (years) at primary insult	1	3	1.5	4	3
Sex	Male	Male	Male	Male	Male
Nationality	Indian	Indian	Indian	Indian	Indian
Presenting complaint	Dyspnea (NYHA Class 3)	Non-specific chest discomfort	Exertional chest pain, occasional palpitation	Exertional chest pain and dyspnea	Occasional chest tightness
IVIG treatment	No	No	No	No	No
Aspirin prophylaxis	No	No	No	No	Yes
LVEF in echocardiography	30%	65%	60%	46%	70%
Wall motion abnormality in echocardiography	LV global hypokinesia	Absent	Absent	LV posterolateral wall hypokinesia	Absent
Coronary artery abnormalities	LMCA cut-off at mid part with collateral filling from right coronary	Aneurysm (internal diameter 9.2 mm) at proximal RCA	Aneurysm of LMCA (diameter measuring 12 mm)	Aneurysm of LCX (8.8 mm) followed by severe obstruction of LCX and OM1	Fusiform dilatation (5 mm) of LMCA at its trifurcation up to ostio-proximal LAD



**Figure 2:** (a) Coronary angiogram showing aneurism of osteo-proximal RCA without any feature of stenosis of lumen. (b) Coronary angiogram showing osteo-proximal LMCA aneurism involving upto bifurcation, without any flow limiting obstruction of lumens. (c) Coronary angiogram showing aneurismal dilatation of LCX prior to 1st obtuse marginal (OM 1) branch followed by severe stenosis of LCX and OM 1



**Figure 3:** (a) and (b) 64 slice CT coronary angiography showing fusiform dilatation (5 mm) of LMCA at its trifurcation upto osteo-proximal LAD without any significant stenosis. (RI = Ramus intermedius)

He received conservative treatment for Kawasaki disease without the use of IVIG. He had dilatation of LMCA in the initial echocardiography, which persisted on serial evaluations. A 64 slice CT coronary angiography done this time revealed fusiform dilatation (5 mm diameter) of LMCA at its trifurcation up to ostio-proximal segment of left anterior descending (LAD) artery without any plaque or stenosis [Figure 3a and b]. He was continued with oral aspirin 5 mg/ kg body weight and was asymptomatic thereafter.

## DISCUSSION

Although most commonly found in Asian population, particularly in Japan, Kawasaki disease occurs worldwide. In many areas, it is more common than rheumatic fever and viral myocarditis.<sup>[3]</sup> There is suggestion that both genetic susceptibility and environmental factors may play a role in Kawasaki disease. Infectious origin is suspected for long without identification of any pathogen till date. Its rarity in the first few months of life and in adults

suggests an agent to which the latter are immune and from which very young infants are protected by passive maternal antibodies.<sup>[4]</sup> The genetic basis of susceptibility is currently unknown. Kawasaki disease has 2 phases: An acute phase lasting 1 to 2 weeks, followed by a chronic (“convalescent”) phase.<sup>[5]</sup> Untreated disease usually resolves spontaneously after several weeks.

Kawasaki disease is a generalized systemic vasculitis involving medium and small size blood vessels throughout the body, virtually always involving the coronaries. Arterial remodeling or revascularization may occur in Kawasaki disease with coronary arteritis. Progressive stenosis in the disease results from active remodeling with an intimal proliferation and neoangiogenesis; the intima is markedly thickened and consists of linearly-arranged microvessels, a layer that is rich in smooth muscle cells, and fibrous layers. Several growth factors are prominently expressed at the inlet and outlet of aneurysms where they are activated by high shear stress.<sup>[6]</sup>

4 out of our 5 patients had coronary artery dilatation or aneurysm. Patients with Kawasaki disease-related aneurysms generally remain asymptomatic. They display normal findings on electrocardiograms and stress tests and are at low risk of subsequent myocardial infarction or sudden death. Sometimes, aneurysms persist and become occlusive, thereby increasing the risk of myocardial infarction or sudden death. The risk factors to predict the presence of coronary aneurysms in Kawasaki disease include boys less than 1 year of age, fever lasting longer than 2 weeks, elevated erythrocyte sedimentation rate persisting for more than 4 weeks, and palpable axillary artery aneurysms. The most important predictor of myocardial infarction and other chronic sequelae is aneurysm size.<sup>[7]</sup> The size less than 4 mm in diameter regresses spontaneously

within a short time,<sup>[8]</sup> whereas those larger than 8 mm in diameter are often associated with a stenotic lesion. Factors associated with regression of aneurysm in Kawasaki disease include age less than 1 year, saccular as opposed to fusiform morphology, and distal location.<sup>[8]</sup> Myocardial infarction can occur early or late after the acute phase; therefore, patients should be counseled to avoid atherosclerotic risk factors, and the progress of these patients should be followed into adulthood.<sup>[9]</sup> Coronary artery lesions are dynamic in the late acute and early convalescent phases. The longer the aneurysms or stenotic lesions persist, the less likely they are to resolve. Lesions in the right and left coronary arteries appear to progress differently.<sup>[10]</sup> Massive thrombosis of the aneurysm is seen predominantly in the right coronary artery, usually within 1 year after disease onset. Progressive localized stenosis at the aneurysm inlet or outlet is seen predominantly in the left coronary artery, again usually within 1 year.

Our patients presented with coronary complications 3 to 14 years after the initial attack of Kawasaki disease. Many a time, the initial diagnosis is either missed or not documentable as is the case in our 4<sup>th</sup> patient. Another term related to this is “atypical” or more preferably “incomplete” Kawasaki disease, which is more common in young infants. Here, lack of sufficient signs fails to fulfill the classic criteria of this disease.<sup>[4]</sup> The diagnosis then mostly based on the echocardiographic or angiographic findings of coronary abnormalities. The laboratory findings of incomplete cases appear to be similar to those of classic cases.<sup>[4]</sup> Therefore, although laboratory findings in Kawasaki disease are non-diagnostic, they may prove useful in heightening or reducing the suspicion of incomplete Kawasaki disease.

The goal in treating Kawasaki disease is to control acute inflammation and to prevent serious cardiovascular complications, such as coronary artery disease.<sup>[11]</sup> During the acute phase of illness, aspirin is administered at 80 to 100 mg/kg per day in 4 divided doses together with IVIG 2 g/ kg in a single infusion.<sup>[12]</sup> High dose aspirin continued until day 14 of illness or  $\geq 48$  to 72 hours after fever cessation. When high-dose aspirin is discontinued, clinicians begin low-dose aspirin (3 to 5 mg/kg per day) and maintain it until the patient shows no evidence of coronary changes by 6 to 8 weeks after the onset of illness. For children who develop coronary abnormalities, aspirin may be continued indefinitely.<sup>[4]</sup> Other forms of treatment including glucocorticoids, pentoxifylline, plasma exchange, abciximab, infliximab, cyclophosphamide etc. are being evaluated, but yet to

come as recommendation.<sup>[4]</sup> The most common anti-thrombotic regimen for patients with giant aneurysms is low-dose aspirin together with warfarin, maintaining an international normalized ratio (INR) of 2.0 to 2.5.<sup>[4]</sup> We followed this protocol in our 2<sup>nd</sup>, 3<sup>rd</sup>, and 4<sup>th</sup> patients. The treatment of acute coronary occlusion in patients with Kawasaki disease should target multiple steps in the coagulation cascade. Because no randomized controlled trials have been performed in children, the treatment of infants and children with coronary thrombosis should be done similar to adults.<sup>[4]</sup>

Attempts at excision or plication of the coronary artery aneurysm have not been successful and have caused deaths. Surgical management in Kawasaki disease comprises primarily coronary artery bypass grafts for obstructive lesions.<sup>[13]</sup> Coronary revascularization is recommended for patients with giant or multiple coronary artery aneurysms or significant stenosis. Overall mortality is low for such operations, and graft target sites are easily accessible since most coronary artery lesions occur in proximal segments with little distal involvement.<sup>[14]</sup> *In situ* arterial grafts are preferred because they have an excellent potential for growth with the patient. The indications for coronary bypass graft procedures in children have not been established in clinical trials, but such surgery should be considered when reversible ischemia is present on stress-imaging test results, the myocardium to be perfused through the graft is still viable, and no appreciable lesions are present in the artery distal to the planned graft site.<sup>[4]</sup> According to one older panel of experts, surgical revascularization may be considered under the following conditions: Severe occlusion of the main trunk of the LMCA, severe occlusion of  $> 1$  major coronary arteries, severe occlusion in the proximal segment of the LAD, collateral coronary arteries in jeopardy, or all of the above.<sup>[15]</sup>

Along with the technical advancement, more and more cases of Kawasaki diseases are going to be diagnosed. There is also a trend of an increasing incidence of this disease. Therefore, we shall need to follow up more such cases and upgrade our knowledge regarding this condition. As coronary artery sequelae of Kawasaki disease can be a cause of ischemic heart disease even in adults, heightened awareness of this possibility is required for adults with coronary lesions but without coronary risk factors.

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