Different Facets of Coronary Artery Pathology in Kawasaki Disease

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Abstract: Kawasaki disease is an idiopathic vasculitis that still challenges clinicians 50 years after it was first reported. Its most concerning feature is the involvement of the coronary artery which may manifest in diverse degrees of severity and extent. The authors describe three cases of Kawasaki disease with different coronary artery outcomes and one challenging case, in which the coronary artery involvement, although not confirmed, fits within the Kawasaki's disease spectrum.

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Key words: Kawasaki disease; coronary stenosis; coronary aneurysm

Introduction

Kawasaki disease is a systemic vasculitis, whose most feared complication is coronary artery involvement.[1]

Factors such as male gender, younger age at onset, and prolonged fever have been linked to the development of coronary artery aneurysms, the majority of which regress. However, some aneurysms, particularly giant aneurysms, tend to persist and are related to coronary artery stenosis or occlusion later in life.[2,3]

Intravenous immunoglobulin therapy reduces the incidence of coronary artery lesions from 20-25% to 3-5%, particularly if administered early in the disease process.[3,4]

The aim of this report is to add insight to possible coronary artery involvement and different types of lesions secondary to a systemic vasculitis of still unknown cause. Informed consent was obtained in all cases.

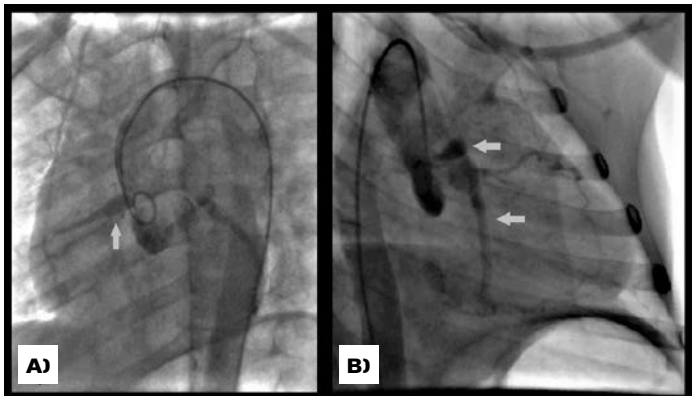

Figure 1. (A) Left anterior oblique aortic root angiogram showing a saccular aneurysm in the proximal region of the right coronary artery measuring 6.0 x 11.0 mm (arrow); **(B)** Right anterior oblique aortic root angiogram revealing a dilated anterior descending artery (4.0 mm) (lower arrow), with saccular aneurysm of the right coronary artery overlapping the aortic root (upper arrow).

Case 1

A five-year-old boy with refractory Kawasaki disease developed bilateral proximal coronary artery aneurysms within the first 10 days of the disease, the largest in the right coronary artery, with a diameter of 6.0 mm (Z-score of +9.16). He required a further immunoglobulin dose and, eventually corticosteroids before the inflammatory process settled. The aneurysms persisted on echocardiogram and a year later, a coronary artery angiogram (**Figure 1**) revealed a significant, right coronary artery saccular aneurysm with moderate dilatation of the anterior descending artery.

To date, the lesions persist with a right coronary artery saccular aneurysm (Z-score of +7.15) on a transthoracic echocardiogram, consistent with a 4.1 type of coronary abnormality according to the American Heart Association risk classification system.[1] The patient is now 11 years old, is asymptomatic, and on anti-platelet therapy. A treadmill stress test and adenosine stress cardiac magnetic resonance have shown no signs suggestive of cardiac ischemia.

Case 2

A 4-month-old baby boy with Kawasaki disease presented with early onset bilateral coronary artery aneurysms (the largest in the proximal region of the anterior descending artery measuring 6.0 mm (Z-score of +16.22). He displayed clinical improvement on intravenous immunoglobulin, but the coronary artery lesions persisted. Six months post admission, a coronary artery angiogram showed only mild right coronary artery enlargement.

At the age of 10 years, a new coronary artery angiogram (**Figure 2**) showed a severe stenotic lesion in the middle segment of the right coronary artery, as well as a rich arterial collateral network arising from this vessel. The patient is asymptomatic on double anti-platelet therapy. A treadmill stress test and dobutamine stress echocardiography showed no evidence of cardiac ischemia.

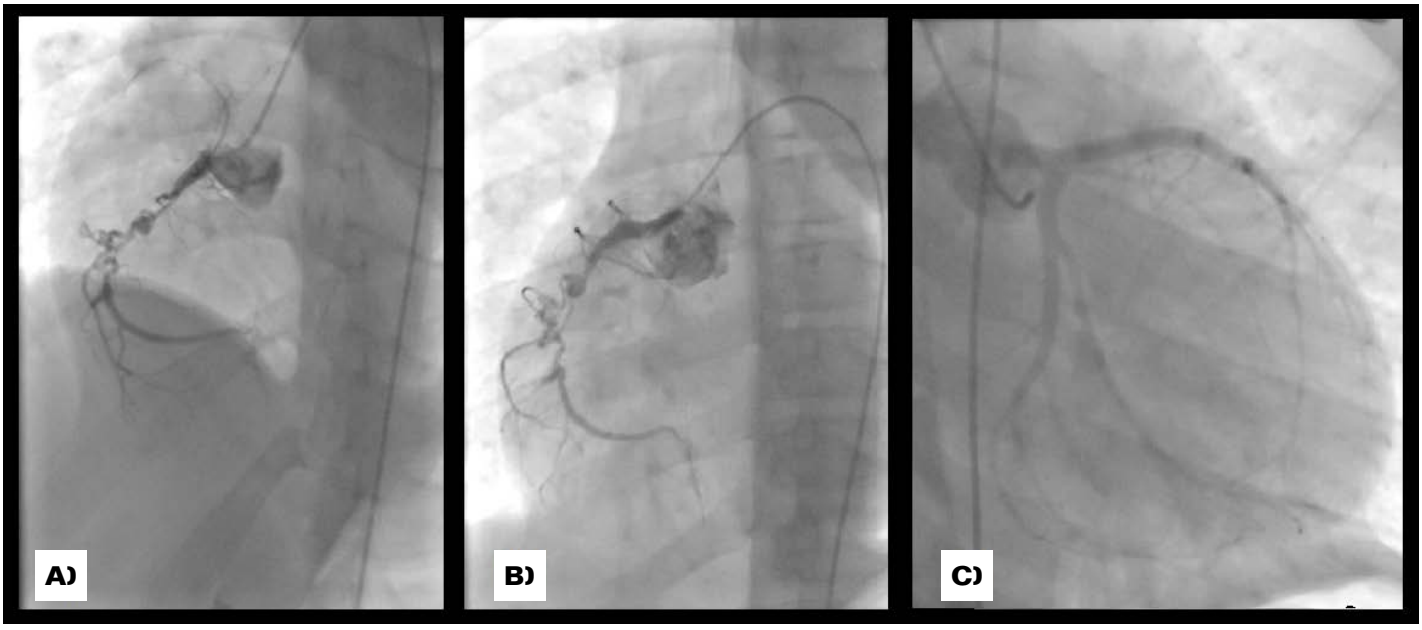

Figure 2. (A and B) Selective right coronary artery angiogram revealing dilation of its proximal segment (4.0 mm) with significant stenosis of the middle segment and a rich arterial collateral network; **(C)** Left coronary artery angiogram showing dilation of the common trunk (4.6 mm), as well as of the proximal segments of the anterior descending artery (3.2 mm) and the circumflex artery (3.3 mm).

Case 3

A 6-year-old boy with refractory Kawasaki disease required 2 cycles of intravenous immunoglobulin, antiplatelet and systemic corticosteroid therapy, and showed on day 11 significant ectasia of both coronary arteries: the right coronary artery measured 3.8 mm (Z-score of +4) and left coronary artery 4.1 mm (Z-score of +3.5).

He was discharged home on day 13 on antiplatelet therapy, but was readmitted twelve days later with fever. The echocardiogram showed worsening of the coronary artery ectasia (**Figure 3**): the right coronary artery measured 6 mm (Z-score of +9.7), the circumflex artery 3.8 mm (Z-score of +2.7), and the left anterior descending artery 7 mm (Z-score of +13). He was started on cyclosporin, systemic corticosteroids, as well as anticoagulant and antiplatelet therapy. Fever resolved promptly but his inflammatory markers took eight days to normalize.

During follow-up the coronary ectasia did not regress and a CT angiogram was carried out, showing, in addition, the presence of giant coronary artery with no significant stenotic lesions. Further investigation showed dilatation of the proximal superior mesenteric artery and small fusiform dilatation of the anterior communicating artery (**Figure 4**). A treadmill stress test showed no signs of ischemia.

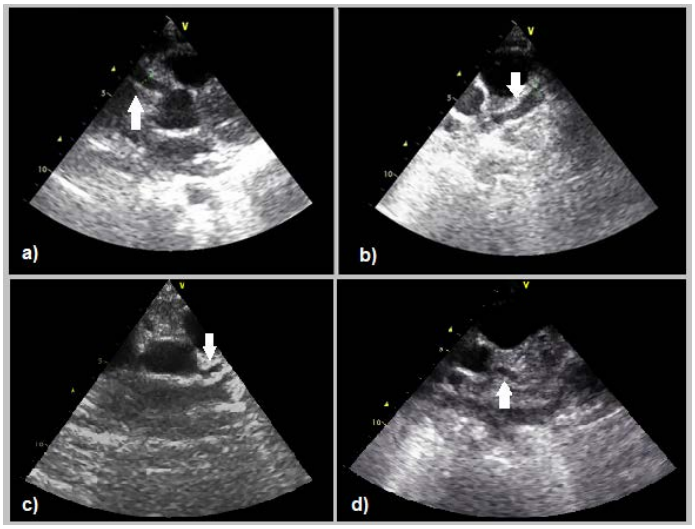

Figure 3. Parasternal short axis view of echocardiogram showing: **(A)** Right coronary artery measuring about 6 mm (Z-score of +9.7); **(B)** Left anterior descending artery of 7 mm (Z-score of +13); **(C)** Left coronary artery and bifurcation; **(D)** Circumflex artery measuring around 3.8 mm (Z-score of +2.7).

Case 4

A 71-year-old man with history of long-term hypercholesterolemia and systemic hypertension was admitted with a myocardial infarction. The coronary artery angiogram (**Figure 5**) revealed diffuse dilatation of both coronary arteries and branches with impaired filling and complete occlusion of the middle segment of the left anterior descending artery.

Although from his past medical history we were unable to confirm previous Kawasaki disease, the findings were suggestive.

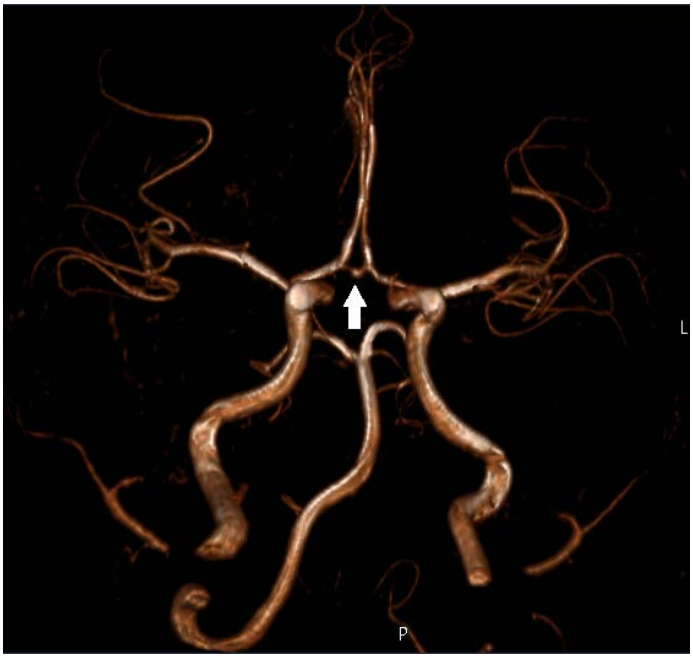

Figure 4. Small fusiform dilatation of the anterior communicating artery.

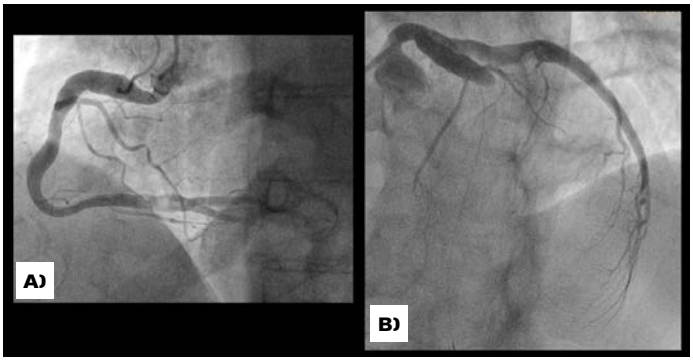

Figure 5. (A) Right coronary artery selective angiogram showing diffuse ectasia, with the proximal segment measuring 10.0 mm and the middle segment measuring 7.0 mm; **(B)** Dilated left coronary artery on selective angiogram showing total occlusion of the middle segment of the anterior descending artery. The proximal segments of both circumflex and anterior descending arteries are 10.0 mm wide.

Discussion

Coronary artery lesions and subsequent ischemic heart disease are the most feared, possibly fatal, complications of Kawasaki disease.[5] Coronary ectasia, aneurysm, or narrowing can be seen in approximately 4% of the children treated with intravenous immunoglobulin.1 Immunoglobulin resistance and/or the occurrence of giant aneurysms are well-known risk factors for persistent lesions and further complications,[2,6] as previously shown.

In fact, the most important predictor of myocardial infarction is aneurysm size. Lesions with a Z-score ≥2.5 to <5 in diameter usually regress spontaneously within a short period, whereas giant aneurysms (Z-score ≥10 or absolute dimension ≥8 mm) are often associated with coronary artery stenosis on follow-up.[1,7] Age at presentation less than 1 year, saccular in contrast to fusiform aneurysms, and distal location are associated with persistent lesions.[7] These features were present in Case 2, which developed significant stenosis in early infancy.

Long-term effects of cardiovascular sequelae of Kawasaki disease were studied by Kato et al., in the pre-immunoglobulin era. They concluded that the incidence of coronary aneurysm formation just after the acute phase was 24.6%, half of which showed regression after 2 years. About 38% of the persistent coronary lesions eventually developed coronary artery stenosis. Ischaemic heart disease occurred in 4.7%, myocardial infarction in 1.9% and death in 0.8% of total cases, the latter one with evidence of coronary artery stenosis previously.[6]

Regarding our adult patient's case, coronary artery ectasia is found in about 3-8% of angiographic studies, very rarely affecting all three vessels. With the advent of intravascular ultrasound about 50% of cases are attributed to atherosclerosis, while 10 to 20% are related to inflammatory diseases or connective tissue disorders, such as Kawasaki disease, Ehlers-Danlos syndrome, or ANCA-related vasculitis. A small percentage of cases are believed to be congenital in aetiology.[8] Based on his age, it is likely that our patient had atherosclerotic related changes. However, due to its extent, we cannot exclude a previous inflammatory insult as the cause of the coronary artery ectasia.

Many cases of fatal and non-fatal myocardial infarction in adults have been attributed to "missed" KD in childhood. Among adults <40 years of age with suspected myocardial ischemia who underwent coronary angiography, nearly 5% had lesions consistent with late sequelae of Kawasaki Disease.[1] ■

Note: Coronary artery Z-scores according to Montreal data: Dallaire F, Dahdah N. New equations and a critical appraisal of coronary artery Z scores in healthy children. J Am Soc of Echocardiogr. 2011;24(1):60-74.

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REFERENCES

1. McCrindle BW, 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.
2. Kuo H-C. Preventing coronary artery lesions in Kawasaki disease. *Biomed J.* 2017;40(3):141-146.
3. Daubeney P, Rigby M, Niwa K, Gatzoulis M. *Pediatric Heart Disease: A Practical Guide*; 1st Edition; Wiley-Blackwell; November 2012; ISBN: 978-0-727-91861-1
4. Agarwal S, Agrawal DK. Kawasaki disease: Etiopathogenesis and novel treatment strategies. *Expert Rev Clin Immunol*. 2017;13(3):247-258.
5. You-quan W, Hao Y, Yong-sheng K. An adult case of severe coronary artery lesions caused by Kawasaki disease diagnosed by coronary angiography. *Heart*. 2011;97(Suppl 3):A211.
6. Kato H, Sugimura T, Akagi T, et al. Long-term consequences of Kawasaki disease. A 10- to 21-year follow-up of 594 patients. *Circulation*. 1996;94(6):1379-1385.
7. Mandal S, Pande A, Mandal D, Sarkar A, Kahali D, Panja M. Various coronary artery complications of Kawasaki disease: Series of 5 cases and review of literature. *J Cardiovasc Dis Res.* 2012;3(3):231-235.
8. Mavrogeni S. Coronary artery ectasia: From diagnosis to treatment. e-*Hellenic J Cardiol*. 2010;51(2):158-163.