CASE REPORT: A THREE-MONTH-OLD BOY WITH INCOMPLETE KAWASAKI DISEASE AND EARLY SUPER-GIANT CORONARY ANEURYSM RESULTING IN DETRIMENTAL CARDIAC FUNCTION

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Abstract. Kawasaki disease (KD) is an acute systemic vasculitis involving medium-sized arteries, especially the coronary arteries. A coronary artery aneurysm is the most common complication of this disease. A super-giant coronary aneurysm is defined as an aneurysm in which the coronary artery diameter is larger than 10 mm. The incidence of coronary aneurysms in KD is about 25% in untreated KD-cases, and drops to less than 5% after using IVIG administration within the appropriate time. The consequences of coronary aneurysm in KD include coronary thrombosis, myocardial ischemia and rupture of the aneurysm. We report a case of a young male infant who was diagnosed as incomplete KD and developed super-giant coronary aneurysms in the first two weeks of the illness. The aneurysms did not regress over the period. Although he was treated with a combination of antiplatelet and anticoagulant medications, he still had a cardiac complication during the follow-up. This group of patients needs thoughtful follow-up because of the high risk of potentially life-threatening complications.

Keywords: giant coronary aneurysm, Kawasaki disease, complication, management

INTRODUCTION

Kawasaki disease (KD) is an acute systemic vasculitis of unknown etiology. The vasculitis affects small- to medium-sized blood vessels, the critical ones being the coronary arteries. A definite diagnosis and proper management are crucial in preventing complications in the coronary arteries. Those children who do not fulfill most of the clinical criteria or those who show unusual presentations are diagnosed as having incomplete and atypical Kawasaki disease, respectively. Such cases make the diagnosis of KD more difficult, and contribute to a higher incidence of coronary complications.

The incidence of coronary artery aneurysms in KD is about 25% in untreated cases; this drops to less than 5% in IVIG treated within the first 10 days of the disease (McCrindle *et al*, 2007). A giant coronary aneurysm is defined as an aneurysm of which the dilation of the coronary artery exceeds 8 mm in diameter; when the diameter is over 10 mm, it is termed a super-giant coronary aneurysm (Imai *et al*, 2006). There have been many case reports of coronary artery thrombosis, myocardial infarction and sudden death following the formation of coronary aneurysms in KD (Suda *et al*, 2011). Careful management

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therefore plays a critical role in patients who have coronary aneurysms.

CASE REPORT

A previously healthy, 3-month-old boy with 5 days of fever was admitted to a regional hospital. Although a physical examination revealed bilateral conjunctival injection without discharge and generalized erythematous macular rash, no other signs of KD were indicated. A complete blood count revealed hemoglobin of 10 mg/dl, hematocrit of 33%, a white blood cell count of 22,800/mm^3, and a platelet count of 484,000/mm^3. The erythrocyte sedimentation rate was 84 mm/hour. A urinary examination, and the AST and ALT levels, were normal. Supportive treatment was given. On the third day of admission, the urine culture was positive for *Escherichia coli*. Meropenem was given in accordance with a drug sensitivity test.

On the tenth day of the illness, the patient's high-grade fever still persisted. He was referred to a tertiary hospital because KD was suspected. Repeat investigations supported a diagnosis of incomplete KD, and an echocardiogram reported the presence of 18-mm-diameter coronary aneurysms in the left main coronary artery (LMCA) and the right coronary artery (RCA). Intravenous immunoglobulin was not given due to the late diagnosis of the disease. Aspirin and warfarin were started; however, as progressive dilation of the coronary aneurysms was noted in an echocardiogram at the 5-month follow-up, the patient referred to our hospital.

Physical examination at our hospital revealed a 6.3-kg boy with a regular heart rate of 132/minute and a blood pressure of 96/54 mmHg. Neither signs nor symptoms of heart failure were noted, and the cardiovascular examination was normal. A chest X-ray showed an abnormal soft tissue shadow at the left heart border (Fig 1). An electrocardiogram demonstrated no significant abnormality (Fig 2).

An echocardiogram revealed normal intracardiac structure without chamber enlargement, and good biventricular function with normal regional wall motion. In addition, the test identified both a super-giant aneurysm (diameter 20

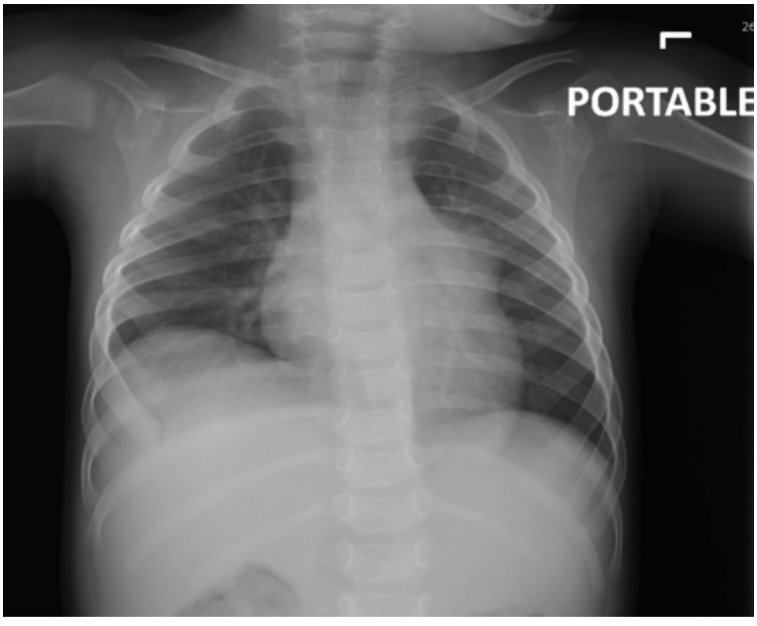

Fig 1– Chest X-ray.

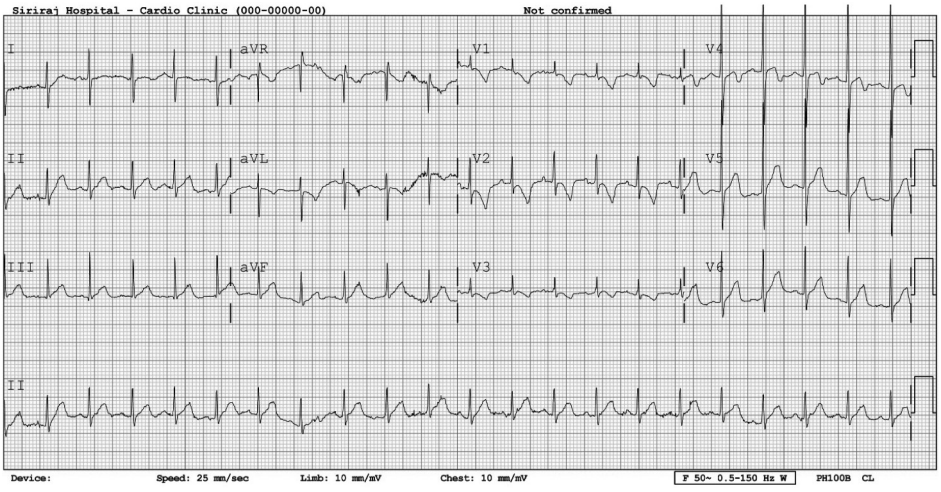

Fig 2– Twelve-lead electrocardiogram.

x 25 mm, with an intraluminal smoky appearance) at the proximal LMCA, and a 4 x 6 mm aneurysm at the proximal RCA. However, no clots were found in either aneurysms. There was no pericardial effusion (Fig 3) and all the cardiac valves were normal.

Because the functional class of the patient was normal and he was doing well without any symptoms, the antiplatelet and anticoagulant medications were continued. The patient underwent a cardiac catheterization and a coronary angiography for hemodynamic study and further evaluation.

The hemodynamic data showed a normal left ventricular end-diastolic pressure, and a normal mean pulmonary artery pressure (10 and 18 mmHg, respectively). The selective coronary angiogram demonstrated a super-giant aneurysm of diameter 24 x 30 mm at the LMCA, and a 5.6 x 9.3 mm aneurysm at the mid-RCA. Moreover, the left circumflex artery (LCX) was normal, but the left anterior descending artery (LAD) was not well-seen. Neither stenosis of these coronary arteries nor clots were revealed.

A computed tomographic coronary angiogram (CTA) was performed to develop a surgical plan. The CTA demonstrated a huge and fusiform aneurysm (diameter 14 x 24 mm) at the LMCA and its bifurcation. The aneurysm wall was severely thickened, but no clots were visible inside it. The LAD and LCX arose from the side of the aneurysm, which was diminutive; the LAD and LCX had no discrete stenosis (Fig 4.1). There was a small, 4 x 6 mm, saccular aneurysm at mid-RCA. A light thrombus was suspected. The distal RCA appeared small with an irregular wall (Fig 4.2).

As the patient was doing well, an elective surgery was scheduled. At the 18-month follow-up, while he was waiting for the surgery, he presented with symptoms of heart failure, and an echocardiogram revealed LV dysfunction. The ejection fraction was decreased from 60% to 53%. He underwent coronary surgery, and the operative finding showed total thrombosis of the aneurysm in the LMCA. The origin of the LMCA was sutured, and the wall of the LMCA aneurysm was partially resected. Coronary bypass surgery from the left internal mammary artery (LIMA) to the LAD, and a saphenous vein graft from the ascending aorta to the LCX, were performed. His LV function was improved 4 months post-surgery.

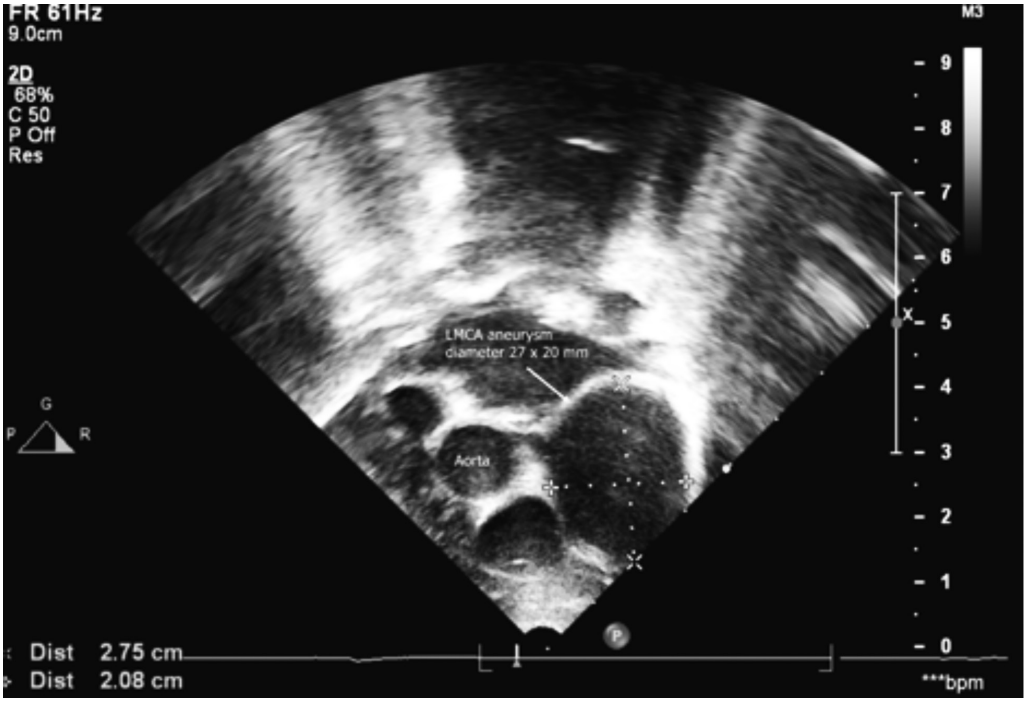

Fig 3.1– Echocardiogram of LMCA aneurysm (subcostal view).

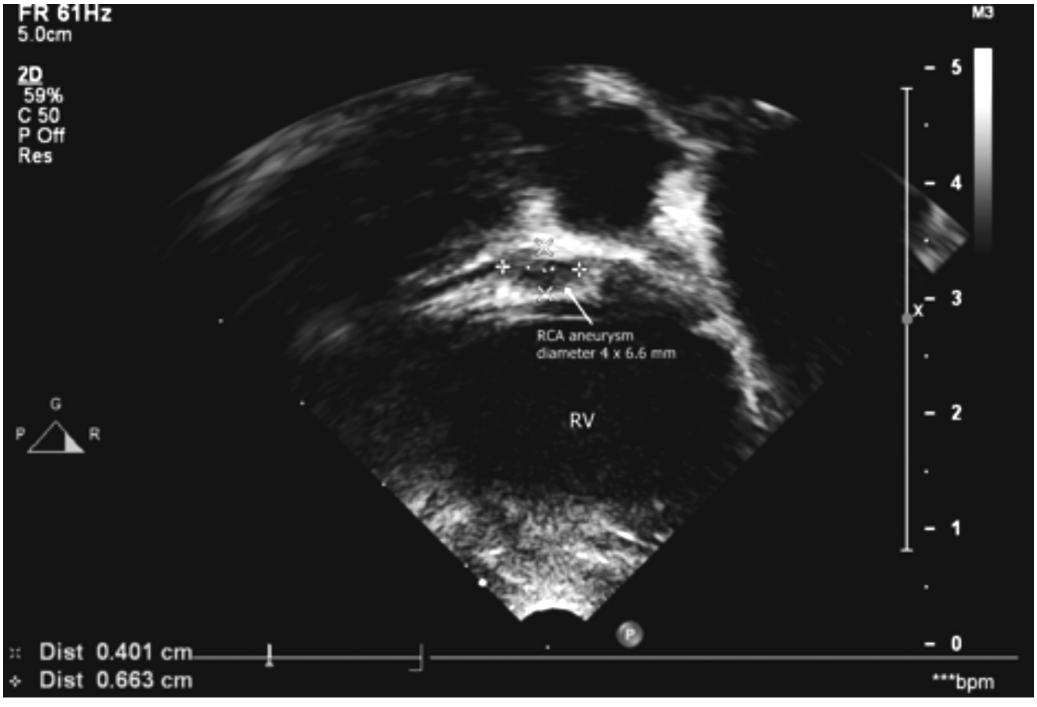

Fig 3.2– Echocardiogram of RCA aneurysm (subcostal view).

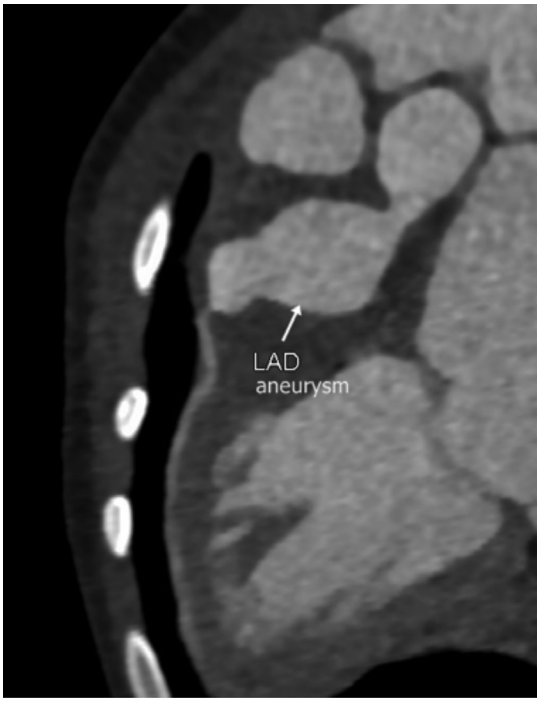

Fig 4.1– Computed tomographic coronary angiogram, LAD aneurysm.

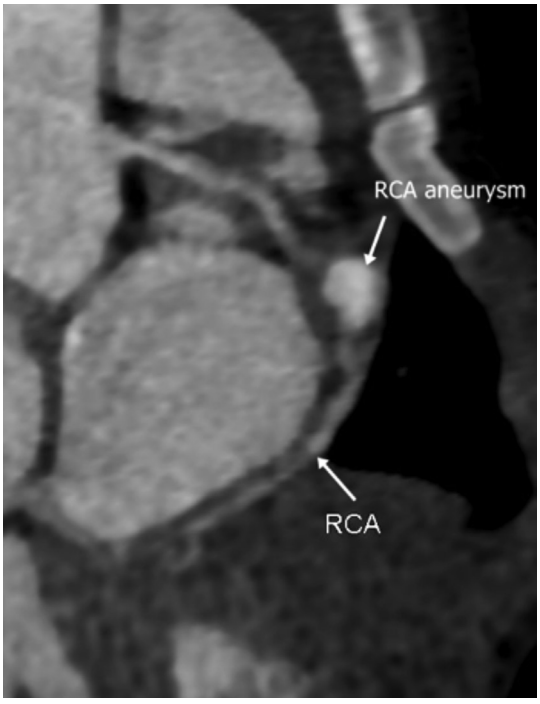

Fig 4.2– RCA aneurysm.

DISCUSSION

Unfortunately, there are no laboratory tests specifically for KD. According to the latest AHA guidelines (McCrindle *et al*, 2017), the diagnosis of classical KD requires fever plus at least 4 criteria, but incomplete KD does not. Physicians should consider this disease in small children presenting with prolonged fever of more than 5 days. It is important to make a diagnosis of KD within 10 days of the onset of the fever because timely management is crucial to the prevention of cardiovascular complications. The long-term prognosis of KD is determined by cardiac sequelae (Dillon *et al*, 2010).

The cardiac complications of KD are coronary aneurysms, decreased coronary arterial compliance, myopericarditis, arrhythmias, valvular regurgitation, myocardial infarction, and sudden cardiac death. The most common and decisive complication is a coronary aneurysm. KD patients less than 6 months or more than 5 years of age, and incomplete KD patients, have a high risk of cardiac complications stemming from a late diagnosis and delayed treatment. Patients who are resistant to IVIG therapy are also at high risk of developing these complications (Eleftheriou *et al*, 2014).

Coronary artery aneurysm is found in 0.3%-5% of adult patients undergoing coronary angiography. The major causes are atherosclerosis, KD, and infectious emboli. In children, KD is the main cause, followed by congenital malformation of the coronary arteries. Kawasaki patients who have persistent aneurysms beyond 8 weeks should have long-term follow-up. These aneurysms can regress: Kato *et al* (1996) reports that 55% of small or moderately-sized aneurysms completely regress within 2 years. The mechanism of regression is remodeling of the vessels with fibrosis and proliferation of subendothelial tissues

(Sasaguri and Kato, 1982; Takahashi *et al*, 1987). Various prevalences of giant coronary aneurysms resulting from KD have been published, ranging from 1% to 2.2%; unfortunately, giant aneurysms never resolve completely (Kato *et al*, 1996). The overall survival rates from giant coronary aneurysms due to KD are 95% at 10 years, 88% at 20 years and 88% at 30 years. Fifty-five percent of KD patients have a cumulative catheter and/or surgical intervention, and 16% have myocardial infarction (Suda *et al*, 2011).

The complications of a giant aneurysm in children can be coronary thrombosis, myocardial ischemia, and rupture of the aneurysm. The mechanisms of thrombus formation inside the aneurysm are the slow flow of the blood and the irregular internal surface of the aneurysmal wall. Thrombus can develop in the aneurysm despite appropriate anticoagulant therapy (Saga *et al*, 1995). Yuan (2012) reported the incidence of thrombosed coronary aneurysms in Kawasaki patient is 30%. If coronary thrombosis, stenosis or occlusion develop, myocardial infarction can occur. Common sites of the coronary obstruction are the LAD, followed by the LMCA, RCA and LCX, respectively (Chanthong *et al*, 2005; McCrindle *et al*, 2007). Giant coronary artery aneurysms frequently result in coronary artery stenosis or obstruction in the next 1 to 20 years, and the aneurysmal diameter is an important predictor of myocardial infarction. There is no evidence of coronary thrombosis earlier than 1 year (Yeu *et al*, 2008), and Kato *et al* (1986) also reported a 4.7% incidence of myocardial infarction in KD patients with aneurysm. Myocardial ischemia and infarction may occur in the absence of coronary stenosis, and they are usually ascribed to thrombotic occlusion or distal microembolization.

Rupture of the aneurysm is a rare complication, but has a poor prognosis. Only eleven cases were reported in the past 15 years (Miyamoto *et al*, 2014). This study suggests that patients with enlarging coronary aneurysms should be monitored closely. The optimal time for surgery is within a month of the onset of the fever, especially in cases with a giant aneurysm larger than 10 mm with rapid, progressive enlargement.

Owing to the high risk of unfavorable outcomes of coronary artery surgery on young children, the literature has mentioned multiple strategies to prevent complications from giant coronary aneurysm, including medication and cardiac catheterization.

As for medical management, Kawasaki patients with persistent coronary aneurysm after 6 to 8 weeks of illness should be given a low dose of aspirin (3-5mg/kg/day) until the coronary artery diameter has regressed to normal size. Physicians should also consider giving patients with a giant aneurysm long-term antiplatelet therapy combined with either warfarin (target INR 2.0-2.5) or low molecular-weight heparin (Newburger *et al*, 2004). Under medical management, a giant coronary aneurysm exhibits various progression patterns.

The surgical treatment of a coronary aneurysm post KD includes coronary artery bypass grafting (CABG), aneurysm plication, or heart transplantation. The indications for surgery in these patients are a giant aneurysm, significant stenosis with calcification, and thrombus formation in the coronary arteries. A coronary artery bypass graft is indicated in patients with severe obstructive lesions, and in younger children who have ischemic changes with multivessel disease (Muta and Ishii, 2010). The challenges of coronary bypass surgery in children are young children (especially less than 2 years old), and long-term patency of a venous graft (Kitamura, 2002). Coronary arterial aneurysm plication is performed in patients with giant aneurysms without significant obstruction (Eleftheriou *et al*, 2014). Only 0.6% of the patients need heart transplantation (Yuan, 2012).

Percutaneous coronary angioplasty is indicated for localized severe stenotic lesions not

involving the ostia. The outcome is unfavorable compared with CABG. Waki and Baba (2006) reported using a polytetrafluoroethylene (PTFE)-covered stent to treat an eight-year-old boy with a giant aneurysm and coronary stenosis post KD to improve the blood flow in the giant aneurysm to laminar pattern.

Our patient was a 3-month-old male infant presenting with prolonged fever and having a positive urine culture for *Escherichia coli*. He did not meet the diagnostic criteria for Kawasaki disease at presentation. The diagnosis of Kawasaki disease was not made until the 12th day of the disease, and IVIG was not given during that time. Given the patient's age and sex, the deferral of the diagnosis at the regional hospital and the inadequate treatment in the intervening period placed him at high risk of developing coronary aneurysms. A giant aneurysm developed in the first 10 days of the patient's illness, without regression. His risk level was 5.1, according to the current AHA guidelines (McCrindle *et al*, 2017). A combination of a low dose of aspirin and warfarin was given. He did not have symptoms of myocardial ischemia, which correlated with the investigations conducted during the first year of follow-up; however, he had clinical signs and symptoms of heart failure and LV dysfunction, demonstrated by echocardiogram, 6 months later. He underwent coronary bypass surgery, and had a favorable outcome.

In conclusion, we report a young male infant with super-giant aneurysms who had coronary thrombosis and LV dysfunction, despite adequate antiplatelet therapy combined with anticoagulant during 18 months of follow-up. This group of patients needs thoughtful follow-up because of the high risk of potentially life-threatening complications.

REFERENCES

Chanthong P, Sriyoschati S, Durongpisitkul K, Soongswang J, Laohaprasitiporn D, Nana A. Coronary artery bypass graft in Kawasaki disease patients: Siriraj experience. *J Med Assoc Thai* 2005;88 (Suppl 8):S197-202.

Dillon MJ, Eleftheriou D, Brogan PA. Medium-size-vessel vasculitis. *Pediatr Nephrol* 2010;25:1641-52.

Eleftheriou D, Levin M, Shingadia D, Tulloh R, Klein NJ, Brogan PA. Management of Kawasaki disease. *Arch Dis Child* 2014;99:74-83.

Imai Y, Sunagawa K, Ayusawa M, *et al*. A fatal case of ruptured giant coronary artery aneurysm. *Eur J Pediatr* 2006;165:130-3.

Kato H, Ichinose E, Kawasaki T. Myocardial infarction in Kawasaki disease: clinical analyses in 195 cases. *J Pediatr* 1986;108:923-7.

Kato H, Sugimura T, Akagi T, *et al*. Long-term consequences of Kawasaki disease. A 10- to 21-year follow-up study of 594 patients. *Circulation* 1996;94:1379-85.

Kitamura S. The role of coronary bypass operation on children with Kawasaki disease. *Coron Artery Dis* 2002;13:437-47.

McCrindle BW, Li JS, Minich LL, *et al*. Coronary artery involvement in children with Kawasaki disease: risk factors from analysis of serial normalized measurements. *Circulation* 2007;116:174-9.

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:e927-e99.

Miyamoto T, Ikeda K, Ishii Y, Kobayashi T. Rupture of a coronary artery aneurysm in Kawasaki disease: a rare case and review of the literature for the past 15 years. *J Thorac Cardiovasc Surg* 2014;147:e67-9.

Muta H, Ishii M. Percutaneous coronary intervention versus coronary artery bypass

grafting for stenotic lesions after Kawasaki disease. *J Pediatr* 2010;157:120-6.

Newburger JW, Takahashi M, Gerber MA, *et al*. Diagnosis, treatment, and long-term management of Kawasaki disease: the Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease, Council on Cardiovascular Disease in the Young, American Heart Association. *Circulation* 2004;110:2747-71.

Saga T, Shirotani H, Shinohara T. Surgical treatment for coronary and iliac arterial lesions in a case of Kawasaki disease. J *Thorac Cardiovasc Surg* 1995;43:57-9.

Sasaguri Y, Kato H. Regression of aneurysms in Kawasaki disease: a pathological study. *J Pediatr* 1982;100:225-31.

Suda K, Iemura M, Nishiono H, *et al*. Long-term prognosis of patients with Kawasaki disease complicated by giant coronary aneurysms: a single-institution experience. *Circulation* 2011;123:1836-42.

Takahashi M, Mason W, Lewis AB. Regression of coronary aneurysms in patients with Kawasaki syndrome. *Circulation* 1987;75:387-94.

Waki K, Baba K. Transcatheter polytetrafluoroethylene-covered stent implantation in a giant coronary artery aneurysm of a child with Kawasaki disease--a potential novel treatment. *Catheter Cardiovasc Interv* 2006;68:74-7.

Yeu BK, Menahem S, Goldstein J. Giant coronary artery aneurysms in Kawasaki disease--the need for coronary artery bypass. *Heart Lung Circ* 2008;17:404-6.

Yuan SM. Cardiac surgical procedures for the coronary sequelae of Kawasaki disease. *Libyan J* 2012;7:19796.