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Original Article

Missed Kawasaki disease in an infant presenting with a giant coronary artery aneurysm with nocturnal awakening symptoms in adolescence: a case report

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Abstract: Herein is described a 11-year-old child who was thought to have Kawasaki disease (KD) as an infant and presenting with nocturnal awakening symptom. Echocardiography and coronary artery CT angiography (CTA) confirmed coronary artery aneurysms (CAA). The patient once had similar presentations of KD and wasn't treated with intravenous immunoglobulins as an infant, which suggested that the diagnosis and treatment of KD was probably missed. He successfully underwent surgical coronary angioplasty and didn't awake in the night again. Although the KD is usually described as an acute self-limiting disease, a subset of patients, especially those with a missed diagnosis, carry a higher and longtime risk for coronary artery problems, like the CAA. Meanwhile, the CAA frequently remains clinically silent and could not be noted until the patients have cardiovascular manifestations.

Keywords: Kawasaki disease, coronary artery aneurysms

Introduction

Kawasaki disease (KD), a systemic vasculitis which predominantly affects coronary arteries, has become a common cause of acquired heart disease in the pediatric population although it was originally thought to be self-limited [1]. Currently, the diagnosis of KD is still made on clinical criteria and there is no specific diagnostic tests or pathognomonic clinical features for this disease. Moreover, approximately 15-20% of KD patients, especially in children younger than 6 months, have atypical or incomplete forms of KD [2]. Due to these, many KD patients can be missed diagnosed or treated, and these patients have a higher incidence of coronary artery abnormalities and more long term consequences, like coronary artery aneurysms (CAA). Furthermore, CAA frequently remains clinically silent for decades. Notwithstanding, KD patients with the CAA carry a lifelong risk for coronary artery thrombosis, myocardial ischemia and infarction. Thus, any children presenting with a protracted fever of unknown origin or other similar symptoms of KD should be suspected of having this disease and physicians should be increasingly involved in the management of these patients.

Case presentation

An 11-year-old boy was referred to our hospital due to low sleep efficiency, which presented as the nocturnal awakening symptom and lasted for nearly 3 months. In the past 1 month, the awakening symptom occurred more frequently, about 3-4 times every night. After waking up, he felt very flustered and fatigued, and had difficulty returning to sleep.

Physical examination showed sober consciousness and normal body temperature with no edema, no bilateral bulbar conjunctivitis, no skin rash or fissured lip. Audible heart murmur was not found and the neurological examination was normal. Blood tests showed the level of B-type natriuretic peptide (BNP) was normal (123.0 pg/mL, normal range 0-125 pg/mL); White blood cell (WBC) count was 5,030/mm^3

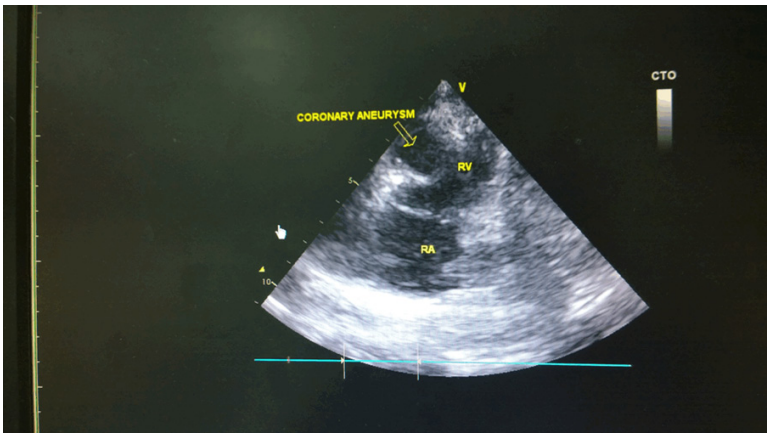

Figure 1. Echocardiography before surgery showing a giant coronary aneurysm in the RCA, the widest part of which presenting as a large cystic mass adjacent to the right ventricle (arrow). RCA: right coronary artery; RA: right atrium; RV: right ventricle.

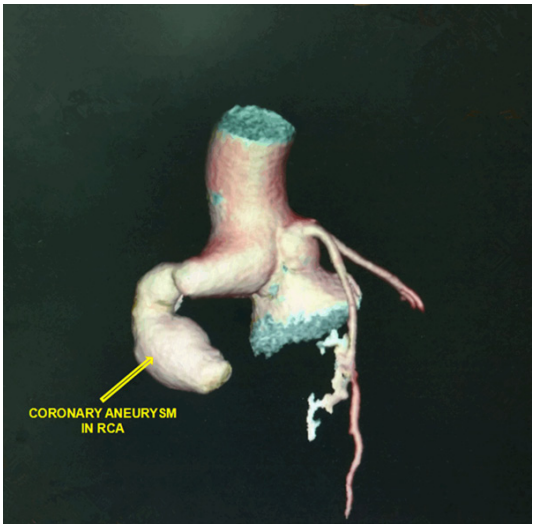

Figure 2. Coronary artery CT angiography before surgery showing a giant coronary aneurysm (phyllodes) in RCA (arrow), and a mild myocardial bridge in left anterior descending branch. RCA: right coronary artery.

with 49% lymphocyte, and platelet (PLT) count was 143,000/mm^3. Also, transaminases and myocardial enzyme were all within normal limits. Altogether, there were no obvious features in this patient. However, dynamic electrocardiogram showed sinus arrhythmia and incomplete right bundle branch block. Interestingly, echocardiography showed severely ectatic right coronary artery (RCA), whose initial diameter was 12.3 mm and maximum diameter was 21 mm with Z scores of 11.8 and 20.4 (based on international standards), respectively [3]; The widest part of the RCA presenting as a large cystic mass adjacent to the right ventricle (**Figure 1**); The location of main coronary artery and the left ventricle systolic function were normal. Coronary artery CT angiography (CTA) revealed occlusions within giant aneurysm (phyllodes) in RCA, as well as a mild myocardial bridge in left anterior descending branch (LAD). Neither calcified aneurysms nor occlusion in the coronary artery was found during the angiography (**Figure 2**).

He had no modifiable risk factors for coronary artery disease, such as hypertension, diabetes, obesity, smoking, or dyslipidemia. The phenomena were noticed that he once had a persistent fever up to 40°C for 7 days and been treated with oral amoxicillin + clavulanic acid because of the otitis diagnosis by the pediatrician ten years ago. Also, transient rash and "bloodshot" eyes appeared during that period. Possibly, the diagnosis and treatment of KD was missed at that time. Since then, the patient did not present any heart discomfort symptoms. In order to rule out the atherosclerosis and systemic arteritis (like nodular arteritis and Takayasu arteritis), lipid profile and inflammatory biomarkers like C-Reactive Protein (CRP) level were assessed, as well as antinuclear antibody and total complement were all tested normal or negative.

At this time, the patient was diagnosed with Kawasaki disease and coronary artery aneurysm according to the American Heart Association (AHA) criteria [4]. He consequently was referred for a surgical coronary angioplasty, and received intravenous immunoglobulin (IVIG: one bolus of 2 g/kg), aspirin (5 mg/kg/day), dipyridamole (3 mg/kg/day). The surgery was uneventful and resulted in complete resolution of the symptom of nocturnal awakening resolution. The patient was finally discharged with low-dose aspirin (5 mg/kg/day) and dipyridamole (3 mg/kg/day). He is being regularly monitored to check the size of the coronary arteries. A echocardiography scheduled 7 months later revealed that the aneurysm of RCA was disappeared, and the diameter of the initial RCA and the widest part of RCA once before

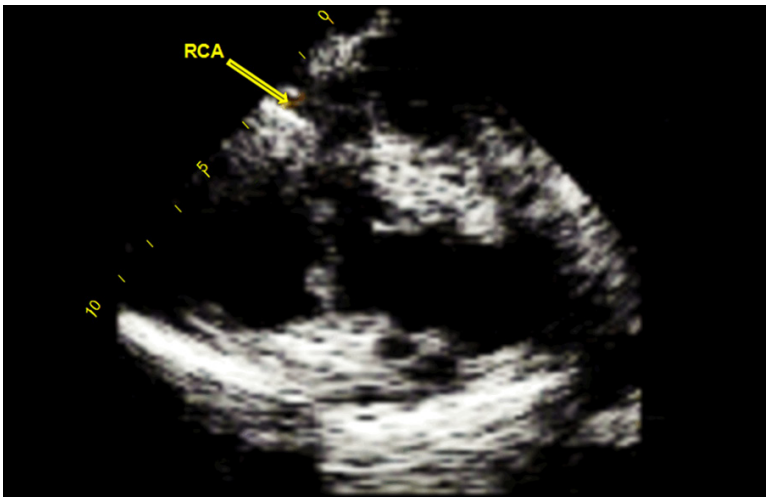

Figure 3. Echocardiography after discharging showing the initial diameter of RCA was 6.3 mm and the widest part before surgery became 2.9 mm now (arrow). RCA: right coronary artery.

the CTA were 6.3 mm (z-score 4.56) and 2.9 mm (z-score 2.64), respectively (**Figure 3**).

Discussion

Kawasaki disease is an acute self-limiting childhood vasculitis and predominantly affects coronary arteries, which is the most important clinical manifestation of the disease, varying from dilation and stenosis to aneurysm. Coronary artery aneurysms (CAA), one of the most common cardiovascular manifestations, often develops within 7 days after fever onset [1]. However, data on follow-up of children with KD revealed that a subset of KD patients went on to develop permanent changes in coronary arteries and resulted in clinical sequelae such as the myocardial ischemia and myocardial infarction in older age [5-11]. As reported, CAA's were noted in 6.7% of patients younger than 40 years with a probable or definitive history of KD by the coronary angiography due to symptoms of myocardial ischemia [6]. In other words, CAA can remain clinically silent for decades until the complications like myocardial ischemia or infarction appears. The clinical sequelae of the KD patients with CAA identified in our literature are summarized in **Table 1**. Our patient, who once had a highly suspicious history of KD like the fever, rash, and "bloodshot" eyes, presented with giant CAA which was highly suspicious for KD though no specific diagnostic test that was used to make a retrospective diagnosis. These data suggest the KD should be considered when marked ectasia or aneurysm of proximal coronary arteries is seen in relatively younger patients who lack other risk factors for coronary artery disease.

The symptoms of the patient with the CAA could be various, either silent or unusual fussiness, vomiting, shock, and even death [2, 12-19]. As reported, more than 13.5% of the patients presented with dizziness symptom related to decreased cardiac output and arrhythmia, 50% of the patients presented with chest pain due to myocardial infarction, and approximately 24% of the patients suffered sudden death [20]. Notwithstanding, the nocturnal awakening symptom aforementioned in our case has not been reported, although unprovoked nocturnal awakenings have been reported to be independently and positively related to the severity of coronary artery disease in multivariate regression analyses [21]. The symptoms of KD patients with CAA identified in our literature are summarized in **Table 2**.

The management of the KD with CAA could be guided by common sense and an appreciation of uncertainty about the cardiovascular outcome. Lifelong aspirin is recommended in the patients with KD who develop coronary artery dilatations. A combination of aspirin and oral anticoagulant should be used for patients with large aneurysms (>8 mm) and sluggish blood flow due to the highly risk of thrombosis. Although decisions regarding the need for revascularization and the optimal mode of revascularization are often difficult and tailored to the patient's clinical status, candidacy for different forms of revascularization should be considered in the KD patients with large and giant aneurysms (Z Score ≥10 or Absolute Dimension ≥8 mm) because progressing coronary artery aneurysms is a major contributor to unexpected morbidity and mortality [4, 22]. The aforementioned case presented a good recovery after the surgery. However, as the child becomes older, it is still important to educate about the particular coronary artery or cardiac issues.

Table 1. Summary of clinical sequelae reported in KD patients with CAA

Ref.	Age (years)	Sex	Age at onset of KD (years)	CA presence	Clinical sequelae
5	35	Male	ND	Ectatic proximal LAD (6 mm)	Myocardial infarction
	40	Male	ND	Ectatic proximal LAD (6 mm)	Myocardial ischemia
	30	Male	ND	Proximal ectasia of LAD	Sudden death
	38	Male	ND	Marked ectasia of proximal LAD	Myocardial ischemia
6	18	Male	11	Dilatations of LAD	Myocardial ischemia
7	5	Male	5	Aneurysm of the LAD	Sudden death
8	32	Female	30	Dilatation of LCA (7 mm)	Alive and well
9	6	Male	5	Aneurysmal dilatation of LAD	Alive and well
10	1.5	Male	1.5	Fusiform aneurysms of CA	Ischemic stroke
11	2	Male	1	Left coronary artery aneurysms with thrombosis	Myocardial infarction

Note: CAA, coronary artery aneurysm; ND, not described; LAD, Left anterior descending; LCA, left coronary artery.

Table 2. Summary of the symptoms reported in the patients with CAA

Ref.	Age (years)	Sex	Symptoms	CA presence
12	3	Female	Retropharyngeal edema, shock syndrome	Dilatation of the LCA
2	0.5	Male	Fever, irritability	An aneurysm of the RCA and an ectasia of the LAD
13	61	Male	Cardiac arrest	Giant CAA involving the LAD, left circumflex, and RCA
14	74	Male	Angina	RCA aneurysm (70 mm) which oppressed the right atrium and ventricle
15	0.4	Male	Shock	Dilatations of RCA (maximal diameter of 9mm)
16	10	Female	No remarkable symptoms	Dilation of the RCA and LCA
17	24	Male	Shortness of breath	Dilatation of the RCA (7.9mm) and LAD (5mm)
18	0.1	Male	Intermittent fever, seizure	An aneurysm of the LCA (3.4 mm)
19	0.3	Female	Fever, vomiting	Dilated RCA, LAD and circumflex artery down to the ventricular apex

Note: CAA, coronary artery aneurysm; LAD, Left anterior descending; LCA, left coronary artery; RCA, right coronary artery.

Disclosure of conflict of interest

None.

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