Coronary artery aneurysms caused by Kawasaki disease in an adult: A case report and literature review

Ying He, Hao Ji, Jian-Chang Xie, Liang Zhou

BACKGROUND
Kawasaki disease (KD) is a self-limiting febrile illness and an acute vasculitis with an unknown origin. It predominantly affects children aged < 5 years. KD is the common cause of acquired heart disease in children. We here report a case of KD in an asymptomatic young female patient diagnosed with multiple coronary aneurysms with calcification.

CASE SUMMARY
A 29-year-old female patient admitted to Hangzhou First People's Hospital with coronary artery abnormality identified for 1 wk. The patient was asymptomatic; however, chest computed tomography occasionally revealed strip-like dense shadows in the coronary sulcus. After coronary angiography and Doppler echocardiography, the final diagnosis was coronary artery aneurysms (CAAs) caused by KD. Although the patient was asymptomatic with no history of KD in childhood, the definitive diagnosis was CAAs caused by KD. The patient was administered anticoagulant, and surgical treatment was recommended.

CONCLUSION
KD potentially causes CAAs in 25% of untreated cases, primarily occurring in the proximal portions of the coronary arteries.

Key Words: Kawasaki disease; Coronary artery aneurysms; Coronary vasculitis; Coronary angiography; Case report

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Core Tip: Kawasaki disease (KD) is the self-limited febrile illness and predominantly affects children < 5 years of age. Here, we report a case of KD in a young girl with coronary artery aneurysms, but with no symptoms. Coronary artery aneurysms occur primarily in the proximal portions of the major coronary arteries in KD, which may result in myocardial infarction. Patients should be diagnosed and treated immediately to obtain a favorable prognosis.

INTRODUCTION

Kawasaki disease (KD) is an acute vasculitis with an unknown cause and predominantly affects children under five years[1]. More than 60 countries have reported cases of KD. Notably, KD has a significant ethnic variation. For instance, Asian/Pacific Islanders have the highest incidence of 29.8 in 100000 children under five years. Nevertheless, the incidence in white children is only 13.7 in 100000[2].

Moreover, according to a 2015 Japanese KD survey, the incidence rate of KD was 330.2 in 100000 children[3,4]. Typical clinical features of KD include fever persistence for five days or more, bilateral conjunctival congestion, changes in lips and oral cavity, polymorphous exanthema, the changes of peripheral extremities, as well as acute non-purulent cervical lymphadenopathy[5]. In the acute phase, erythema and edema manifest in the hands, whereas feet and periungual desquamation was remarkable[1]. Nonetheless, patients diagnosed in adulthood are asymptomatic with no history of KD in childhood. They instead present coronary disease without other findings. Coronary artery aneurysms (CAAs) are another KD complication, mostly occurring in the proximal coronary artery. Most KD patients with CAAs are symptomatic. We here report a rare case of KD in an asymptomatic young female with CAAs, and discuss the diagnosis and treatment of KD.

CASE PRESENTATION

Chief complaints

A 29-year-old female patient was admitted to our hospital on April 3, 2019, due to the presence of coronary artery abnormality for one week.

History of present illness

When the patient had a medical check-up one week earlier, a computed tomography (CT) scan of the lungs revealed postoperative cardiac changes. The patient had no obvious discomfort. One day earlier, at the outpatient department of Hangzhou First People's Hospital, echocardiography was performed, and showed coronary artery changes associated with KD. The patient was hospitalized at the Department of Cardiology for further diagnosis and treatment.

History of past illness

The patient reported no history of KD hypertension, diabetes, coronary heart disease, and neurodevelopmental disorders, no history of surgery, and no family history of related genetic disorders.

Personal and family history

The patient had no relevant personal and family history.

Physical examination

On examination, the patient had a temperature of 36.7°C, blood pressure of 131/70 mmHg (1 mmHg = 0.133 kPa), and heart rate of 73 beats/min. The heart rhythm was regular, the heart boundary was not enlarged, and there were no murmurs in each valve area. The whole abdomen was flat without rebound tenderness. Also, no edema was observed in both lower limbs.

Laboratory examinations

Blood routine examination, and liver function, kidney function, coagulation function and autoantibody tests were normal.
**Imaging examinations**

A CT scan of the lungs showed occasional strip-like dense shadows at the coronal sulcus. An electrocardiogram showed sinus arrhythmia and wandering heart rate in the sinoatrial node. Exercise treadmill test showed negative outcomes. To further establish the cause of coronary artery abnormality, the patient underwent Doppler echocardiography and coronary artery computed tomography angiography (CTA). Irregular widening and enhanced wall echo at the beginning of the coronary artery, and multiple CAAs with thrombogenesis were observed (Figure 1). The cause of coronary artery ectasia remained to be determined, and coronary artery changes were associated with KD. And then, CAG revealed CAAs in multiple branches of coronary arteries with thrombosis and calcification (Figure 2). Coronary artery ectasia was observed at the extremity of left main coronary artery. The vessels in the descending proximal left anterior were tortuous with thrombus. The distal vessels were in the myocardial bridge. Moreover, two hemangiomas were observed at the extremity of the left circumflex artery with calcification. In addition, a huge coronary artery aneurysm was in a proximal segment of the right coronary artery with an organized thrombus. The vascular wall was calcified with curved residual blood vessels. There was arteriosclerosis in the distal vessels, narrowing by 30%-40%.

**FINAL DIAGNOSIS**

The final diagnosis was CAAs caused by KD based on coronary angiography and other examinations.

**TREATMENT**

The patient was administered 0.1 g acetylsalicylic acid (ASA) and 75 mg Clopidogrel Hydrogen Sulphate Tablets daily to resist platelets. The patient was also administered Metoprolol Succinate Sustained-release Tablets to control ventricular rate. Further surgical treatment was recommended. However, the patient refused it. Post-discharge medication was adjusted to Rivaroxaban and Metoprolol Succinate Sustained-release Tablets.

**OUTCOME AND FOLLOW-UP**

The patient was followed up for nearly three years. The patient was effectively improved without apparent discomfort. Doppler echocardiography was performed one year after discharge. The inner diameter of the left main coronary artery was 0.4 cm; the inner diameter of the aneurysm near the cross of vessels was 1.0 cm; the inner diameter of the right coronary artery was 0.56 cm (Figure 3). We found no significant changes in coronary arteries with an ejection fraction (EF) value of 0.69. Doppler echocardiography two years after discharge showed no significant changes in coronary arteries with an EF value of 0.64.

**DISCUSSION**

KD is an acute vasculitis with unknown origin and predominantly affects children under five years, resulting in multi-system inflammatory syndrome[1]. It is also known as mucocutaneous lymph node syndrome. KD may be caused by pathogen infection, vaccination, environmental factors, inherited genetic susceptibility, and immune response[6]. The pathological vascular changes of KD are subdivided into three processes[7]. In the early stages of KD, coronary arteries undergo mixed inflammatory cell infiltration. The second is the primary stage of coronary artery injury and aneurysm formation. Fibrosis of blood vessels and myocardium is the third and final stage of coronary artery disease[6]. Over 60 countries have reported cases of KD. Typical clinical features include fever which persists for five days or more, bilateral conjunctival congestion, changes in lips and oral cavity, polymorphous exanthema, changes in peripheral extremities, and acute non-purulent cervical lymphadenopathy[5]. Table 1 shows a review of Clinical Characteristics, Management, and Outcome of Coronary Artery Aneurysm (CAAs) caused by KD; various symptoms were observed[8-20].

Nevertheless, a few patients are asymptomatic with no history of KD in childhood. We here report an asymptomatic 29-year-old female patient who had CAAs caused by KD. After carefully reviewing the coronary artery CTA and coronary angiography images, the cause of CAAs was KD. Therefore, attention should be paid to asymptomatic patients by conducting Doppler echocardiography and coronary angiography to confirm the KD diagnosis. CAAs caused by KD primarily occur in the proximal coronary artery. The diagnostic tests include Doppler echocardiography, magnetic resonance angiography, coronary artery CTA, and coronary arteriography. KD diagnostic indicators include a
Table 1 Review of clinical characteristics, management, and outcome of coronary artery aneurysm caused by Kawasaki Disease in the case report

| Ref. | Age (yr) | Sex | Indication                  | Sites         | Sizes          | FU  | Operation | Antithrombotic therapy | Adjuvant drug | Outcome |
|------|----------|-----|------------------------------|---------------|----------------|-----|-----------|------------------------|---------------|---------|
| Hu et al [9], 2014 | 8 | Male | Ruptured coronary aneurysm | LAD/RCA       | 3.7 mm/5.2 mm | 12 d | NO        | ASA                    | IVIG (2 g/kg), | Dead    |
| Sato et al [9], 2014 | 35 | Male | AMI                          | LAD           | 2.3 mm × 2.0 mm | 9 yr | PCI       | NO                     | NO            | Stable  |
| Matushita et al [9], 2014 | 32 | Male | AMI                          | LAD/RCA       | NA             | 30 yr | PCI       | ASA                    | NO            | Stable  |
| Ikic et al [11], 2014 | 4 mo | NA  | MI                           | LAD/RCA       | 6.5 mm/6.7 mm  | 51 d | NO        | ASA, LMWH              | IVIG (2 g/kg), | Dead    |
| Lua et al [12], 2015 | 17 | Male | MI                           | LAD/LCX/RCA   | NA             | 18 mo | PCI       | ASA, clopidogrel        | Bisoprolol,   | Stable  |
| Chong et al [13], 2018 | 9 | Female | Severe respiratory failure | LAD           | 7 mm         | 8 mo | NO        | ASA, Enoxaparin, warfarin | IVIG (2 g/kg) | Stable  |
| Takai et al [14], 2019 | 3 | Male | Fever                        | RCA           | 8.3 mm       | 3 mo | NO        | ASA, ticlopidine, warfarin | IVIG (2 g/kg), | Stable  |
| Tsuda et al [15], 2020 | 58 | Female | Palpitate                   | LAD           | NA           | NA    | Implantable defibrillator, catheter ablation | ASA         | Beta-blocker, | Stable  |
| Chen et al [16], 2020 | 22 | Male | AMI                          | LMCA          | 18 - 20 mm   | 2 mo  | Heart transplant | Rivaroxaban, clopidogrel | Metoprolol, | Stable  |
| Fujioka et al [17], 2021 | 33 | Female | Postpartum                  | RCA           | 25 mm        | 5 mo  | Resection, CABG | ASA, ticlopidine hydrochloride | NA         | Stable  |
| Wang et al [18], 2021 | 5 mo | Male | Cerebral infarction         | LAD/RCA       | 11 mm × 9 mm/19 mm × 14 mm | 15 mo | NA | ASA, clopidogrel | IVIG (2 g/kg) | Dead    |
| Almashary et al [19], 2021 | 4 mo | NA  | Fever                        | LMCA/LAD/RCA  | 4.6 mm/3.8 mm/4.2 mm | 1 mo | NA | ASA | IVIG (2 g/kg) | Stable  |
| Toyoshima et al [20], 2022 | 14 | Female | AMI                          | LMCA/LAD      | 7.2 mm/4.0 mm | 1 yr | CAbG | warfarin, clopidogrel | Carvedilol, | Stable  |

AMI: Acute myocardial infarction; ASA: Aspirin; CABG: Coronary artery bypass graft; FU: Follow-up period; LAD: Left anterior descending artery; LCX: Left circumflex artery; LMCA: Left main coronary artery; LMWH: Low-molecular-weight heparin; NA: Not available; RCA: Right coronary artery.

Fever that persists for five days or more with at least 4 of the 5 principal clinical features [21]. These principal clinical features include bilateral conjunctival congestion, changes in lips and oral cavity, polymorphous exanthema, changes in peripheral extremities, and acute non-purulent cervical lymphadenopathy [5].

In addition, incomplete KD is evaluated in patients without complete clinical features of classic KD, and diagnosis is confirmed if coronary artery abnormalities are detected [21]. Thus, our patient conforms to the diagnosis of incomplete KD. Regular Doppler echocardiography is also important in the diagnosis. The coronary artery CTA and coronary arteriography show the location and extent of CAAs. We performed the coronary artery CTA and coronary arteriography and confirmed that KD caused CAAs. Noteworthy, CAAs and thrombus in the lumen are severe complications of KD. These complications result in myocardial infarction and ischemic heart disease. The diameter of CAAs greater than or equal to 5 mm has a higher risk of thrombosis [22]. The patient experienced no discomfort; however, CAAs had calcification and thrombosis.
Primary therapy includes intravenous immunoglobulin (IVIG) and ASA. The refractory cases require corticosteroids, tumor necrosis factor (TNF) inhibition, interleukin 1 inhibition, calcineurin inhibition, etc.[1]. IVIG is most effective when used within 10 days of fever onset. Therefore, the risk of CAA decreases from 20%-25% to 3%-5% in patients with appropriate treatment[23,24]. Additionally, ASA should be administered at a moderate dose (30-50 mg/kg/d)[25]. By early adjunctive corticosteroid therapy, patients with a higher risk of poor coronary outcomes can significantly benefit from corticosteroids[26,27]. TNF inhibitors, interleukin 1 inhibition, and calcineurin inhibition are uncommonly used. Primary prevention of thrombosis was fundamental in this patient. ASA and Clopidogrel Hydrogen Sulphate Tablets were administered to resist platelets. We adjusted post-discharge medication to
Rivaroxaban and Metoprolol Succinate Sustained-Release Tablet. Although this therapy did not yield a complete cure, it provided a reference for subsequent treatment strategies, i.e., heart bypass surgery.

In addition, the maximum Z score of proximal LCA or RCA (maximum Z of CA) can be used as an index for long-term follow-up to evaluate the ability of KD patients to achieve coronary perfusion during exercise[28]. Compared with normal children, KD children have a higher prevalence of epilepsy and Tourette’s syndrome[29]. Other functional impairments have also been mentioned, such as facial paralysis, sensorineural hearing and visual loss, ataxia, and behavioral disorders[30].

CONCLUSION
The most significant clinical outcome of KD is inflammation of the coronary arteries. KD can be classified into complete KD and incomplete KD. KD may lead to CAAs in 25% of untreated cases. CAAs occur primarily in the proximal portions of the major coronary arteries in KD, which further results in myocardial infarction. Patients should be diagnosed and treated immediately to obtain a favorable prognosis. More research attention should be paid to asymptomatic KD patients.

FOOTNOTES

Author contributions: The main contributor is He Y; He Y wrote the manuscript; Ji H and Xie JC were the treating physicians and were responsible for revising the manuscript; Zhou L provided assistance during the diagnosis and treatment; Zhou L performed surgery, and Ji H helped analyze the imaging data; all authors read and endorsed the final draft.

Supported by Scientific Research Fund of Zhejiang Provincial Education Department, No. Y202145971.

Informed consent statement: Informed written consent was obtained from the patient for publication of this report and any accompanying images.

Conflict-of-interest statement: All the authors declare that they have no conflicts of interest.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

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Country/Territory of origin: China

ORCID number: Liang Zhou 0000-0003-1996-3088.

S-Editor: Liu JH
L-Editor: Ma JY
P-Editor: Liu JH

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