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ST-segment elevation myocardial infarction in Kawasaki disease: A case report and review of literature

Lee *et al.* A patient with Kawasaki disease presenting with STEMI

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Abstract**BACKGROUND**

Kawasaki disease (KD) is an acute self-limiting febrile vasculitis that occurs during childhood and can cause coronary artery aneurysm (CAA). CAAs are associated with a high rate of adverse cardiovascular events.

CASE SUMMARY

A Korean 35-year-old man with a 30-year history of KD presented to the emergency room with chest pain. Emergent coronary angiography was performed as ST-segment elevation in the inferior leads was observed on the electrocardiogram. An aneurysm of the left circumflex (LCX) coronary artery was found with massive thrombi within. A drug-eluting 4.5 mm× 23 mm-sized stent was inserted into the occluded area without complications. The maximal diameter of the LCX was 6.0 mm with a Z score of 4.7, suggestive of a small aneurysm considering his age, sex, and body surface area. We further present a case series of 19 patients with KD, including the current patient, presenting with acute coronary syndrome (ACS). Notably, none of the cases showed Z scores; only five patients (26%) had been regularly followed up by a physician, and only one patient (5.3%) was being treated with antithrombotic therapy before ACS occurred.

CONCLUSION

For KD presenting with ACS, regular follow up and medical therapy may be crucial for improved outcomes.

Key Words: Kawasaki disease; Acute coronary syndrome; ST elevation myocardial infarction; Coronary angiography; Percutaneous coronary intervention; Case report

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Core Tip: Kawasaki disease can lead to coronary artery aneurysms. The presence of a coronary artery aneurysm increases the risk of developing acute coronary syndrome. However, we found that proper long-term medical care or regular examination had not been provided to the 19 previously reported patients in this case series. Thus, based on the Z scores, our data highlight the importance of meticulous care by a cardiac specialist.

INTRODUCTION

Kawasaki disease (KD) is one of the most common causes of acute self-limited febrile illnesses resulting in vasculitis during childhood^[1]. The incidence of KD is the highest in boys under 5 years of age and in East Asia^[2,3]. In an Asian nationwide cohort, the annual risk of coronary complications was 2.4% during 2000-2010, and the incidence of acute myocardial infarction (MI) was 1.52%^[4]. KD can cause multiple complications throughout the body^[5]. Cardiac complications, such as coronary artery aneurysm, heart failure, MI, and arrhythmia, lead to significant morbidity and mortality^[6]. KD-related vasculitis destroys medium-sized arteries, among which coronary arteries are commonly influenced. Coronary arteries affected by KD have been reported to develop coronary artery aneurysm (CAA) in up to 25% of untreated patients^[6-9], whereas the incidence drops to approximately 4% when treated with intravenous immunoglobulin (IVIG)^[10,11]. Such aneurysms are also known to be associated with coronary artery diseases^[12].

Moreover, as the size of the aneurysm increases, the prevalence of MI also increases^[6]. At four United States hospitals in San Diego, 5% of patients under 40 years of age with suspected MI who underwent coronary angiography had a history of KD^[11]. Herein, we present a case of a male Korean patient with a history of KD presenting with MI; we also discuss a case series of 19 patients with KD who were subsequently diagnosed with acute coronary syndrome (ACS).

CASE PRESENTATION

Chief complaints

A 35-year-old man visited the emergency room (ER) complaining of chest pain.

History of present illness

His symptoms were intermittent once a day before. His chest pain (numeric rating scale of 7) worsened 2 h before visiting the ER.

History of past illness

He had no significant medical history except for the diagnosis of KD at 2 years of age.

Personal and family history

He was currently not under any medications. His coronary risk factor was a 5-year smoking history. The patient had quit smoking at the time of visiting the emergency room.

Physical examination

His physical examination was normal, with a blood pressure of 121/72 mmHg, pulse rate of 72 beats per minute, body temperature of 36.8 °C, and a respiratory rate of 18 breaths per minute.

Laboratory examinations

¹ The electrocardiogram (ECG) demonstrated a sinus rhythm with ST-segment elevation in leads II, III, aVF, and V4-V6 (Figure 1A). Initial blood tests reported that creatine kinase myocardial band (CK-MB), troponin-I, ⁶ high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol values were 4.970 ng/mL, 236.95 pg/mL, 42 mg/dL, and 204 mg/dL, respectively.

Imaging examinations

The initial echocardiogram revealed akinesia of the posterolateral wall from the base to the mid-left ventricle and hypokinesia of the anterolateral wall from the base to the mid-left ventricle without thinning, leading to moderately ⁵ reduced left ventricular systolic function [left ventricular ejection fraction (LVEF): 47%]. Emergent ³ coronary angiography (CAG) showed aneurysmal dilatation of the proximal segment of the right coronary artery (RCA) and total occlusion of the distal left circumflex (LCX) and obtuse marginal (OM) arteries with sluggish flow (Figure 1A and B).

⁷ **FINAL DIAGNOSIS**

The final diagnosis of the presented case was ST elevation myocardial infarction due to CAA after KD.

TREATMENT

Thrombosuction was performed on the LCX lesion, although the coronary blood flow was not improved. Further, subsequent extensive balloon angioplasty using a 2.5 mm × 15 mm balloon to the distal LCX and OM did not restore the blood flow. Intravascular ultrasound (IVUS, TVC imaging system™, Infraredx, Inc, Bedford, MA) showed a diameter of 6.0 mm CAA in the distal LCX with a hazy material, suggestive of thrombosis (Figure 2A). Based on these findings, the patient's Z score was 4.7 (height 167 cm and body weight 73.5 kg), classified as being within a small aneurysm range^[13]. We were not able to further advance the IVUS catheter into the OM owing to resistance and angulation (Figure 2D). However, after IVUS examination, fluoroscopy showed thrombolysis in

myocardial infarction 2 flow to the distal LCX with massive thrombi (Figure 2B). A drug-eluting stent (Genoss™ 4.5 mm × 23 mm, Genoss, Suwon, Korea) was successfully inserted (nominal pressure: 10 atm, inflated up to 10 atm) into the culprit lesion without a no-reflow phenomenon (Figure 2C). We decided to insert a drug-eluting stent instead of a bare metal stent because anticoagulation was not considered unless the presence of a giant aneurysm of a Z score > 10 was determined^[14].

OUTCOME AND FOLLOW-UP

After the procedure, dual antiplatelets (100 mg aspirin and 90 mg ticagrelor twice daily) and statins (10 mg rosuvastatin) administration was initiated. Owing to the high thromboburden, the patient was treated with intravenous heparin for 48 h post-percutaneous coronary intervention (PCI). ST-segment elevation disappeared in the ECG performed 8 h after the procedure. Cardiac markers were observed to peak at 12 h (CK-MB > 300 ng/mL and troponin-I > 25000 pg/mL) post-PCI. The patient was discharged after 3 d without any additional events and was prescribed dual-antiplatelet therapy, nicorandil, and a statin. He is being followed up regularly in the outpatient department. However, the follow-up echocardiogram 6 mo after the initial PCI showed no interval change in LVEF and regional wall motion abnormality. Coronary computed tomography (CT) performed one year later showed good patency at the LCX stent area and ectatic aneurysm in all coronary arteries (Figure 2D and E). The patient is currently being followed up in the outpatient clinic without any events since 2 years while under dual-antiplatelet therapy.

DISCUSSION

Diagnosis of coronary artery abnormalities and Z score for primary prevention of coronary artery disease

Large CAAs are associated with a high risk of adverse cardiovascular (CV) events.^[15, 16] Thus, the identification of a potential CAA is crucial for patients diagnosed with KD. Coronary artery abnormalities arising from KD in children can be identified in most cases

by echocardiogram^[17]. However, visualizing the distal segment of coronary arteries can be challenging. Other imaging modalities can be legitimate options, such as cardiac CT angiography, cardiac magnetic resonance imaging, or CAG. Statistical Z scores have been devised to objectively assess the size of the CAA based on the patient's age, sex, and body surface area^[14]. Thromboprophylaxis is determined by the Z scores according to the recent guidelines^[14]. The classification of Z scores of CAA and their corresponding thromboprophylaxis recommendations are summarized in Table 1 and Figure 3^[14].

Long-term management of KD-related CAA and primary prevention for coronary artery thrombosis

The primary treatments for KD include IVIG and aspirin^[18]. A meta-analysis showed that the use of high-dose IVIG reduced the progression to CAA^[19]. In patients with IVIG-resistant KD, corticosteroids and infliximab can be used for the prevention of CAA. Once a CAA is formed, the goal is the primary prevention of coronary thrombosis. Although there is no study comparing the outcome in those with or without appropriate follow up and imaging surveillance to date, it is recommended by expert consensus^[14]. Further studies are required to demonstrate the usefulness of imaging surveillance. Additionally, despite the limited evidence on the benefit of the use of antiplatelets, it is recommended by expert consensus as well^[14]. The benefit of additional anticoagulation in patients with Z score-based giant aneurysms was, however, demonstrated by a previous study^[20]. Anticoagulation is recommended in such patients^[14]. For small CAAs ($2.5 \leq Z \text{ score} < 5$), low-dose aspirin is recommended^[14], whereas a combination of aspirin and warfarin is recommended for those with giant aneurysms ($Z \text{ score} > 10$) (Table 1 and Figure 3)^[21]. Additionally, it is recommended to set the international normalized ratio (INR) value of 2-3 with a daily INR check until the target INR is reached when the patient is first diagnosed with a giant aneurysm. Monthly INR testing is to be followed unless the patient is sick or undergoes a change in their medication or diet^[14].

Case review of patients with KD presenting with MI

We reviewed the papers published regarding KD patients presenting with ACS. We first searched the PubMed database (search last updated in December 2021). The keywords were Kawasaki disease and acute coronary syndrome and case report. Among the 337 studies that were found, we excluded cases with patients under the age of 18 years and papers written in languages other than English. Among the 30 cases with these conditions, we further selected 18 cases from 14 publications with definite diagnoses (19 cases from 15 publications, including our own) (Table 2)^[22-35].

In this case series, the average age of initial KD diagnosis was 3.2 ± 2.2 years. MI occurred at 28.5 ± 6.3 years of age, and the mean maximal diameter of the CAA was $11.7 \text{ mm} \pm 6.8 \text{ mm}$. Among a total of 19 patients, 4 (21.1%) patients underwent coronary stenting (1 Korea and 3 Japanese patients). After the diagnosis of KD, regular follow-up until adulthood was only performed in 5 of 19 cases (26.3%). Although a regular follow-up is recommended by expert consensus, there is limited evidence as to whether it translates to improved outcomes. However, a more concerted effort in this arena appears to be crucial, as patients diagnosed with KD are often neglected or lost to follow-up even in specialized centers. In a survey of 104 United States pediatric hospitals of patients with KD, only 10% of patients were referred to a cardiologist, and the majority of patients (79%) did not undergo a third echocardiographic evaluation, suggesting that such patients were lost to follow-up^[36]. Moreover, only 4% of patients were managed according to the guidelines in a United States tertiary hospital^[36]. A Japanese survey of KD experts in 2014 showed that 90% of the respondents considered it necessary for patients with KD to consult a cardiologist regularly in adulthood if there was a coronary artery lesion^[37]. More than 40% of patients did not undergo regular examinations during adulthood.

In patients with CAA, if the Z score is greater than 2.5, a transition to adult cardiac follow-up is required at the age of 16 to 18 years^[9]. Notably, none except for the current patient among the 19 patients presented with Z scores (Table 2). The maximal diameter was measured in only 12 patients, including the current patient, out of 19 patients (63%). However, considering that the mean maximal diameter ($11.7 \text{ mm} \pm 6.8 \text{ mm}$) of the 12

patients was above 10 mm, the CAAs were giant aneurysms by definition and were indicated for both anticoagulation and antiplatelet therapy. This suggests once more that physicians worldwide may be relatively unaware of the Z score or the importance of maximal diameter in relation to long-term outcomes^[36]. Our patient also had a Z score of 4.7 in his LCX; however, the patient was not evaluated until MI occurred and was not being treated with antithrombotic therapy.

Additionally, most KD patients may not be under thromboprophylaxis treatment despite it being indicated. Although there is limited information regarding the percentage of patients under antithrombotic therapy in the literature, our study of the case series suggests that a very low percentage of patients (1 out of 19 patients, 5.3%) underwent thromboprophylaxis (Table 2). Since the disease is rare, it appears that physicians are commonly unaware of the long-term evaluation and management of KD, such that governmental initiatives may be necessary to educate and promote physicians and caregivers for both primary and secondary prevention.

The use of IVUS in ACS patients with KD

The use of IVUS is recommended during PCI in KD patients with ACS by expert consensus^[14]. PCI with IVUS can confirm the exact vascular pathology and diameter of vessel^[38]. The IVUS helps stent deployment during coronary intervention and anticoagulation after procedure^[14]. In our patient, we used IVUS during the procedure because we did not have a good visual on distal OM and to confirm the underlying pathophysiology.

CONCLUSION

From the current case and the case series of 19 KD patients who presented with ACS, we found that proper long-term medical care had not been provided, including regular examination and medical therapy. For KD presenting with ACS, regular follow up and medical therapy may be crucial for improved outcomes.

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