Case Report

Recurrent Kawasaki Disease Complicated by Giant Coronary Aneurysms Showing Only Two Clinical Manifestations

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We herein report a recurrent case of Kawasaki disease (KD) complicated by giant coronary aneurysms that developed only fever and slight conjunctival injection. A 3-year-old boy developed a cough and fever for one day and was referred to us because of a strong inflammatory reaction. He had a history of complete KD previously, and was treated with intravenous immunoglobulin therapy (IVIG) 7 months ago with no coronary arterial lesion afterward. However, this time, he had a cough and chest X-ray showed consolidation; therefore, we suspected bacterial pneumoniae and started antibiotic therapy. Since this failed to reduce his fever, we administered another antibiotic drug, which was also ineffective. Echocardiography was performed on day 7 from onset and revealed bilateral coronary arterial aneurysms, the appearance of which resembled a string of beads. Based on this finding, he was diagnosed with incomplete KD and IVIG, cyclosporine A, and aspirin were administered. Fever improved 12 hours later, but recurred at 36 hours. Due to the possibility of the further expansion of coronary arterial aneurysms, he was transferred to another hospital for plasma exchange.
Patients with recurrent KD are known to be at risk of coronary arterial lesions. However, since the present case only exhibited 2 main manifestations, making an accurate diagnosis was not straightforward. Therefore, the recurrence of KD needs to be considered in children with fever and a history of KD.

Keywords: Kawasaki disease, recurrence, coronary aneurysm, incomplete Kawasaki disease

Introduction

Kawasaki disease (KD) is an acute, self-limited febrile vasculitis. The disease was initially described in Japan in 1967.[1] The goal of therapy in the acute phase is to reduce inflammation and prevent arterial damage.

In the 1970s–80s, KD patients were treated with acetylsalicylic acid (ASA) and prednisolone. The efficiency of high-dose intravenous immunoglobulin (IVIG), at 400 mg/kg/day for 5 days followed by a single high dose of 2 g/kg, was introduced; that is now the primary treatment for KD.[2]

According to the recent 25th nationwide survey in Japan, there were 32,528 KD patients in 2017–8, 94.6% of whom received IVIG therapy. However, 35 patients (0.11%) developed giant coronary arterial aneurysms in the acute phase.

We herein report a case of recurrent KD complicated by giant coronary aneurysms that exhibited only two of the main manifestations of this condition.

Case

The patient was a 3-year-old boy with an unremarkable family history. He had an earlier episode of KD 7 months before and exhibited 6 clinical features (3 days of fever, conjunctival injection, erythema of the lips, erythema and edema of the hands and feet, rash, cervical lymphadenopathy). He was treated with IVIG (2 g/kg

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for 1 day), two doses of pulsed intravenous methylprednisolone (30 mg/kg/dose), and ASA, since unlikely to benefit from IVIG alone. Fever improved by the end of the IVIG infusion. KD symptoms did not recur. He was discharged on day 11. Echocardiography performed during the hospital stay and in the 1-month follow-up confirmed the absence of coronary arterial lesions.

He eventually presented with a second episode with a cough a few days earlier. He visited the home doctor on the first day of fever and was referred to our hospital due to a strong inflammatory reaction (C-reactive protein level, 10 mg/dL).

His temperature was 38.8°C and SpO_2 98%. Chest X-ray revealed consolidation in the right lower lung. Laboratory data showed a white blood cell count of 25,400/μL with 79% neutrophils, platelets 451,000/μL, albumin 3.5 g/dL and Na 131 mmol/L. His C-reactive protein level was 10.4 mg/dL. His transaminase level was normal, whereas bilirubin was 2.4 mg/dL.

On admission, he exhibited only 2 clinical manifestations of KD (the first day of fever and slight conjunctival injection). We suspected bacterial pneumonia based on his respiratory symptoms, X-ray findings, and laboratory data.

Antibiotic therapy with sulbactam/ampicillin was initiated, but did not attenuate his fever or cough. On day 4, his C-reactive protein level increased to 19.3 mg/dL. Slight conjunctival injection disappeared on day 2, and there were no other symptoms of KD. Therefore, we suspected ampicillin-resistant bacterial infection, and changed sulbactam/ampicillin to ceftriaxone, which was also ineffective.

On day 7, echocardiography to detect the origin of fever showed bilateral coronary arterial aneurysms, the appearance of which resembled a string of beads. There was a 5.6-mm (Z 6.7) aneurysm on the left main coro-

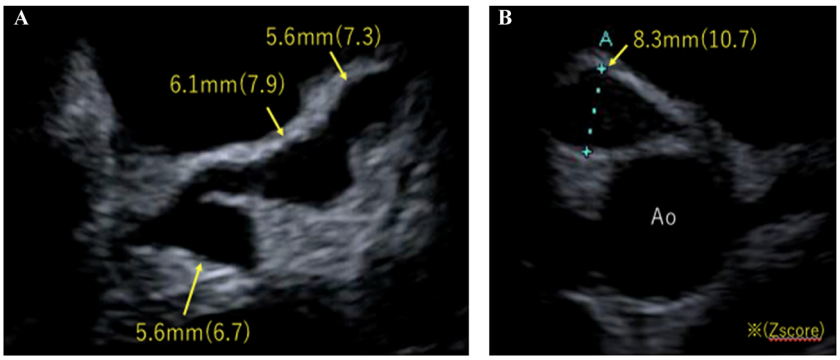

Fig. 1 Parasternal short axis view showing three aneurysms on the left coronary artery (A) and one on the right coronary artery (B) with measurements (mm) (arrows)
Ao, aorta.

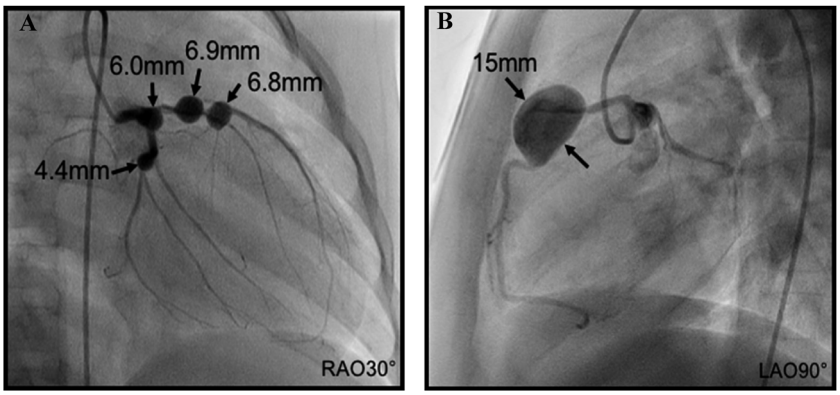

Fig. 2 Angiography one month after the onset of KD showing four medium-sized aneurysms on the left coronary artery (A) and one giant aneurysm on the right coronary artery (B)
LAO, left anterior oblique; RAO, right anterior oblique.

nary trunk (LMT), 6.1-mm (Z 7.9) and 5.6-mm (Z 7.3) aneurysms on the left anterior descending artery (LAD), and an 8.3-mm (Z 10.7) aneurysm on the right coronary artery (RCA) (Fig. 1). Therefore, the patient was diagnosed with incomplete KD and we administered IVIG (2 g/kg) and ASA (30 mg/kg/day). Cyclosporine A (6 mg/kg/day) was also given to reduce inflammation. Fever improved 12 hours after the initiation of IVIG, but recurred at 36 hours. No changes were observed in coronary aneurysms. Due to the possibility of the further expansion of coronary aneurysms, the patient was transferred to another hospital for plasma exchange. Plasma exchange was performed for 3 days, which reduced his fever and C-reactive protein level.

Angiography 1 month later revealed four medium-sized aneurysms on the left coronary artery (6 mm on LMT, 6.9 mm and 6.8 mm on LAD, 4.4 mm on the left circumflex coronary artery) and one giant aneurysm (15 mm) on RCA (Fig. 2).

Discussion

We herein described a case of recurrent KD complicated by giant coronary aneurysms that exhibited only two of the main manifestations of this condition. Two important issues were identified in the present case: recurrence and an incomplete form of KD.

In a recent nationwide survey conducted in Japan, recurrent KD accounted for 4.5% of all cases of KD. Nakamura et al. reported that the risk of coronary arterial lesions was higher with recurrent KD than in its initial onset.[3] Furthermore, the incidence of cardiac complications was significantly higher with recurrent KD, 25.5% in boys and 16.1% in girls, than during its initial onset. In addition, the incidence of giant coronary aneurysms was two-fold higher in recurrent cases, particularly among boys. The present case had these two risk factors for giant coronary aneurysms, and, thus, was considered to be a very high risk case.

A previous study reported that incomplete KD is also a risk factor for coronary arterial lesions due to delays in treatment.[4] Since the accurate diagnosis of KD is often difficult in incomplete cases, the initiation of treatment is delayed, which may bypass the acute phase during which inflammation should be treated. In the present case, the only symptom of KD, other than fever, was slight conjunctival injection. Similarly, a 3-year-old boy with incomplete KD and coronary aneurysms also presented with only fever and conjunctival injection.[5] It was stated that, in incomplete KD, conjunctival injection tends to appear at an early stage.[6] KD can be suspected if there are symptoms of conjunctival injection, even if mild.

Pathologically, coronary arterial inflammation generally starts on the 6–8th day after the onset of KD.[7] Inflammatory cells, neutrophils and macrophages appear in the coronary arterial wall, and damage or destroy the intima, media, adventia, and elastica interna. In cases with severe inflammation in the artery, coronary dilation or aneurysm commonly starts on around 12 days after the disease onset.[8] In the present case, giant aneurysms developed early on day 7 after the onset.

The early presentation of aneurysms in the present case may have been due to the following reasons. At the initial onset of KD, no coronary lesions were detected on echocardiography; however, inflammation might not have completely resolved. The recurrence of KD may have caused secondary damage, leading to the formation of aneurysms. This secondary episode of vasculitis damage to the vascular wall was likely severer than that during the first episode, thus causing coronary dilation and aneurysm at an early stage.

Recent advances in the treatment of KD have decreased the incidence of coronary arterial lesions. However, rare cases of KD with giant coronary aneurysms, similar to the present case, are still being reported.[5] First, it is important to carefully examine patients with fever to see if they have any symptoms that suggest KD, even if they are mild. In addition, performing echocardiography on patients at an earlier stage, particularly those with a history of KD, should result in a more rapid initiation of treatment and prevention of coronary arterial lesions, which will further improve the prognosis of KD.

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Conflict of Interest

There is no conflict of interest to be disclosed in this article.

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