Incomplete Kawasaki Disease Manifesting as Transient Heart Failure in a Previously Healthy Adolescent

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Abstract

Kawasaki disease (KD) is a mucocutaneous lymph node syndrome with important cardiovascular complications which usually afflicts young children. We describe a 16-year-old woman who developed transient heart failure during the acute phase of incomplete KD. The diagnosis was based on the development of coronary aneurysms during heart failure and 2 criteria of the disease. Incomplete KD is a cause, albeit rare, of myocardial dysfunction in human adolescents. Healthcare providers should therefore be aware of the possibility of incomplete KD in patients with heart failure during the course of an acute febrile illness associated with mucocutaneous changes.

Key words: heart failure, incomplete Kawasaki disease, adolescent

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Introduction

Kawasaki disease (KD) is an acute inflammatory disease that primarily afflicts infants and young children (1, 2). Adult onset KD is rare. The etiology of KD is unknown, although KD was first reported by Kawasaki 40 years ago (1). KD is diagnosed clinically using specific diagnostic guidelines (3). The principal symptoms are as follows: I Fever persisting 5 days or more (inclusive of cases in which fever has subsided before the fifth day in response to therapy); II Bilateral conjunctival congestion; III Changes in the lips and oral cavity: reddening of lips, strawberry tongue, and diffuse injection of oral and pharyngeal mucosa; IV Polymorphous exanthema; V Changes in peripheral extremities: reddening of palms and soles, indurative edema in the initial stage, and membranous desquamation of fingertips in the convalescent stage; and VI Acute non-purulent cervical lymphadenopathy. At least 5 of the 6 criteria I-VI should be satisfied for a diagnosis of KD. Patients with four of the principal symptoms also can be diagnosed as KD when coronary aneurysm or dilation is recognized by two-dimensional echocardiography or coronary angiography. However, results from the 20th nationwide surveillance in Japan suggest that the prevalence of atypical (incomplete or suspected) KD patients is 20.2% (4).

Case Report

A previously healthy 16-year-old woman was admitted to the regional hospital for treatment of a fever of unknown origin that had persisted for 4 days. She did not take any drugs. Her body temperature was 39°C, and her pulse was 127 beats per minute (bpm). Her body weight was 46 kg and height 162 cm. Physical examination revealed bilateral conjunctival congestion and tachypnea. No exanthema, enanthema, lymphadenopathy, or arthritis was present. C-reactive protein (CRP), serum alanine aminotransferase (sALT), and serum aspartate aminotransferase (sAST) were elevated at 24.2 mg/dL, 45 IU/L, and 52 IU/L, respectively. Intravenous antibiotic treatment was initiated. Viral and bacterial cultures of blood and urine were negative. Antibiotic treatment had no effect on the patient’s fever or clinical condition. On the fifth day of illness, the patient developed hypoxia with an arterial partial pressure of oxygen of 61.9 mmHg. Chest radiography and echocardiography showed severe congestive...

Figure 1. Bilateral conjunctival congestion.

Figure 2. Chest radiograph obtained on admission showing bilateral pulmonary infiltrates and pleural effusion.

heart failure. Initially, acute myocarditis was suspected. The patient was subsequently transferred to Asahikawa City Hospital. Upon admission, the patient’s body temperature was 38.2°C, pulse was 116 bpm, and blood pressure was 74/52 mmHg. Physical examination revealed bilateral conjunctival congestion (Fig. 1) and gallop rhythm, but no eruption. A chest radiograph showed pulmonary congestion and cardiomegaly (Fig. 2). An electrocardiogram (ECG) showed first-degree atrioventricular block (Fig. 3A). Echocardiography showed diffuse hypokinesis, pericardial effusion, and no dilatation of coronary arteries (Fig. 4A). The patient experienced dyspnea on minimal exertion and wet cough. Examination of urine revealed slight proteinuria. Complete blood count revealed 8,120 white blood cells with shifting to left (stab 29.0% and segmental 65%) and normal platelet count (14.2×10⁴/m³). CRP, erythrocyte sedimentation rate (ESR), sALT, sAST, and brain natriuretic polypeptide (BNP) were all elevated at 33.0 mg/dL, 81 mm/hr, 73 IU/L, 81 IU/L, 434.4 pg/mL, respectively. Hemoglobin was 11.5 g/dL, serum albumin 2.8 g/dL, serum sodium 137 mEq/L, and creatine phosphokinase (CPK) 61 IU/L. During acute phase, there was no increase in the level of CPK. No specific autoantibodies were detected. Viral and bacterial cultures of blood and urine were rechecked, but negative. The patient was treated for congestive heart failure with inotropic agents and oxygen. Small-dose intravenous immunoglobulin therapy (IVIG) 5 g/day for 3 days, a dose which is covered by Japanese medical insurance for severe infection, was administered to address the possibility of myocarditis caused by some viral infection or incomplete KD based on the medical history of fever persisting 5 days or more and bilateral conjunctival congestion. Then, the patient’s circulation gradually improved and body temperature gradually decreased. Although the ECG showed a T wave inversion in the II, III, aVF, and V3-6 leads and first degree atrioventricular block (Fig. 3B) on the seventh day of illness, these parameters also gradually improved (Fig. 3C). On the 12th day of illness, echocardiography showed that the patient’s coronary artery (left main trunk-left anterior descending) was dilated to a diameter of approximately 10 mm (Fig. 4B). Based on this finding, we strongly suspected incomplete KD as the diagnosis and initiated treatment with 200 mg per a day of aspirin. On the 16th day of illness, coronary artery angiography (CAG) revealed aneurysm of the right and left coronary arteries (Fig. 5). Other data from catheterization were within normal limits. Examination of a biopsy specimen from the myocardium revealed a slight hypertrophy and disarray of cardiomyocytes and interstitial fibrosis (Fig. 6). Finally, we diagnosed incomplete KD. The aneurysm of the coronary arteries persisted throughout the entire hospitalization (Fig. 4C). We considered the initiation of warfarin to prevent thromboembolism in giant coronary aneurysms, but did not use it because of menstruation. We have not detected symptoms of heart failure in this patient since then. CAG performed 1 year later revealed persistent aneurysm of the coronary artery and occlusion of a distal coronary artery. However, cardiac function was still normal.

Discussion

To the best of our knowledge, this is the first report in which a previously healthy woman developed transient heart failure during the acute phase of incomplete KD. In this case, the diagnosis of KD was initially difficult because the patient did not fulfill the criteria of KD and was older than typical KD patients and because heart failure, rather than coronary artery involvement, was the predominant clinical manifestation during the acute phase.

Incomplete KD is defined as the presence of 4 or fewer of the principal symptoms of the Japanese diagnostic guidelines, regardless of coronary artery abnormality (7). The
Figure 3. Twelve-lead electrocardiography findings show first-degree atrioventricular block findings upon admission (A). Electrocardiography findings show a T wave inversion in the II, III, aVF, and V3-6 leads and first degree atrioventricular block on the seventh day of illness (B), and these findings gradually improved to the time of discharge (C).

Figure 4. Transthoracic echocardiography upon admission (A), the 12th day of illness (B), and at the time of discharge (C). Parasternal short-axis view shows aneurysm of the left anterior descending artery from the 12th day of illness (arrows).

The present case did not fulfill the diagnostic criteria for KD. This case had just two principal symptoms (fever persisting 5 days or more, bilateral conjunctival congestion) and several other significant findings, such as gallop rhythm, prolonged PR intervals, cardiomegaly, slight increase of serum transaminase, increased ESR, positive CRP, hypoalbuminemia and slight proteinuria. Sonobe et al. reported that the prevalence of incomplete KD is high in patients younger than 1 year and older than 5 years and that patients older than 5 years have a high prevalence of coronary artery abnormalities (7). In addition, the prevalence of coronary artery abnormalities is higher in incomplete KD (18.4%) than in complete KD (14.2%) (7, 8). There are some other known disease processes with a similar clinical presentation such as hypersensitivity drug reaction and toxic shock syndrome (9). She had no staphylococcal infection and no previous any drug intake; therefore we could rule out toxic shock syndrome and hypersensitivity drug reaction. In KD, aneurysms in other medium-sized arteries occur rarely. In this patient, there were no aneurysms in other arteries and no suspicious signs of other disease that might have caused coronary artery aneurysm, such as atherosclerosis, congenital, mycotic disease, and a systemic inflammatory disease including polyarteritis nodosa or systemic lupus erythematosus (10). Therefore, the diagnosis of incomplete KD was appropriate for this patient.

The etiology of KD, especially the mechanism underlying myocardial damage, remains unknown. Several cytokines, including interferon gamma, tumor necrosis factor alpha, interleukin-1, and interleukin-6, are reported to be elevated in the serum of patients with acute KD (5). These cytokines are thought to contribute to myocardial contractile dysfunction. IVIG therapy decreases the levels of these cytokines and is thus expected to improve myocardial function (5). It has been reported that adult KD patients show rapid recovery after therapy with aspirin and IVIG (9, 11, 12). The doses of IVIG which they used were from 0.4 to 2 g/kg/day and the duration of medication was from one day to 5 days (9). The recommended dose for older KD patients has not been established. Therefore, the dose of IVIG, 2 g/kg for 1 day, commonly recommended for children with KD (13) might be too high for an adolescent patient, espe-
Coronary artery involvement is a very serious complication of this disorder, occurring in 11.0% of KD patients (4). In the remote phase of the patients complicated by coronary artery lesion, the major cause of death has been found to be ischemic heart disease due to stenotic lesions resulting from coronary intimal hyperplasia or thrombotic occlusion. Therefore patients with coronary aneurysm due to KD should receive antiplatelet drugs continuously to prevent ischemic heart disease and the formation or growth of thrombi by platelet activation. In the present case, we used aspirin only because of menstruation, but the combined use of aspirin and warfarin is recommended to prevent thromboembolism in patients with giant coronary aneurysms in the recent guideline (13). In conclusion, incomplete KD in adolescents should be considered if the patient has fever and heart failure of unknown origin.

The authors state that they have no Conflict of Interest (COI).

References