

Incomplete Kawasaki disease in an infant presenting with only prolonged fever

Halil Özdemir¹, Aylin Çiftçi², Adem Karbuz¹, Ergin Çiftçi¹, Ercan Tutar³, Semra Atalay³, Erdal İnce¹

Divisions of ¹Pediatric Infectious Diseases, and ³Pediatric Cardiology, ²Department of Pediatrics, Ankara University Faculty of Medicine, Ankara, Turkey. E-mail: doktorhalil@gmail.com

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A 2.5-month-old boy admitted to our hospital with irritability, poor feeding and fever of 12 hours' duration. On physical examination, he was febrile and extremely irritable. Initial whole blood count revealed a hemoglobin level of 10.1 g/dl, white blood count of 17,800/mm³ and platelet count of 454,000/mm³. Erythrocyte sedimentation rate was 80 mm/h and C-reactive protein was 3.96 mg/dl. Biochemical examinations of serum, urinalysis, chest X-ray, and analysis of cerebrospinal fluid (CSF) were normal. He was started on intravenous ampicillin and ceftriaxone empirically for provisional occult bacteremia. His blood, urine and CSF cultures were negative. On the 7th day of the treatment, there were no additional symptoms or findings other than fever. Echocardiography revealed aneurysms in both the left and right coronary arteries. Intravenous immunoglobulin (IVIG) and per oral aspirin were administered, and the fever resolved after IVIG infusion. Two years later, the echocardiography showed disappearing of the saccular aneurysm on the right coronary artery, but the dilatation of the left coronary artery was persisting. In conclusion, incomplete Kawasaki disease should always be included in the differential diagnosis of an infant with persistent fever, especially one younger than three months of age, when the conventional work-up fails to reveal the underlying cause.

Key words: child, incomplete Kawasaki disease, Kawasaki disease, prolonged fever.

Kawasaki disease (KD) is an acute, self-limited vasculitis of unknown etiology that occurs predominantly in infants and young children¹. Frequently, KD is complicated by coronary artery lesions, with coronary artery aneurysms developing in approximately 15–25% of untreated children, making this disease the leading cause of acquired heart disease among children in developed countries².

In this report, we present a 2.5-month-old infant diagnosed as incomplete KD with only prolonged fever.

Case Report

A 2.5-month-old boy was admitted to our hospital with irritability, poor feeding and fever of 12 hours' duration. On the physical examination, he was febrile and extremely irritable. His vital signs included an axillary

temperature of 38.6°C, heart rate of 144 beats per minute, respiratory rate of 48 breaths per minute, and a blood pressure of 72/44 mmHg. The rest of the physical examination was normal. Initial whole blood count revealed a hemoglobin (Hb) level of 10.1 g/dl, white blood cell count (WBC) of 17,800/mm³ (62% neutrophils, 26% lymphocytes, 6% monocytes, and 6% stab cells), and a platelet (Plt) count of 454,000/mm³. Erythrocyte sedimentation rate (ESR) was 80 mm/h and C-reactive protein (CRP) was 3.96 mg/dl. Biochemical examinations of the serum, urinalysis, chest X-ray, and analysis of cerebrospinal fluid (CSF) were normal. He was started on intravenous ampicillin and ceftriaxone empirically for provisional occult bacteremia. His blood, urine and CSF cultures were negative. The next day, his feeding and irritability had improved, but he remained febrile (37-38.5°C). On the

4th day of his follow-up, whole blood count and acute phase reactants were similar to the results of the first day (WBC: 16,700/mm³, Hb: 9.9 g/dl, Plt: 420,000/mm³, ESR: 80 mm/h, CRP: 4.2 mg/dl) and liver function tests were normal (total bilirubin: 0.14 mg/dl, aspartate aminotransferase (AST): 25 U/L, alanine aminotransferase (ALT): 17 U/L, gamma-glutamyl transferase (GGT): 44 U/L). The abdominal ultrasonography was normal.

On the 7th day of the treatment, there were no additional symptoms or findings other than fever. The laboratory work-up established anemia (Hb: 8.3 g/dl), thrombocytosis (Plt: 710,000/mm³), and elevation in the levels of CRP and GGT (8.55 mg/dl and 157 mg/dl, respectively). Although he had none among the following principal manifestations of KD - bulbar conjunctival injection without exudates, changes in the oral mucosa (including red-fissured lips, red mouth and throat, and strawberry tongue), redness and swelling of the hands and feet, erythematous (primarily truncal) rash, or cervical lymphadenopathy - an echocardiogram was done by the pediatric cardiologist to investigate the fever origin. Echocardiography revealed aneurysms in both the left and right coronary arteries (Figs. 1, 2). The width of the saccular aneurysm on the right coronary artery was 3.5 mm (range: 0.9-1.86 mm, Z-score: 7.25) and the width of the fusiform aneurysm on the left coronary artery was 4.5 mm (range: 1.24-2.4 mm, Z-score: 7.6). The antibiotics were stopped and intravenous

immunoglobulin (IVIG) (2 g/kg) and per oral aspirin (80 mg/kg) were administered. The fever resolved after IVIG infusion. Two weeks later, acute phase reactants became negative and the thrombocytosis disappeared, so the dosage of aspirin was reduced to 5 mg/kg. The last echocardiography (2 years after the diagnosis) showed disappearing of the saccular aneurysm on the right coronary artery (width of the right coronary artery: 2.2 mm, range: 1.23-2.31, Z-score: 1.3), but the dilatation of the left coronary artery was persisting (width of the left coronary artery: 3.4 mm, range: 1.62-2.9, Z-score: 2.94). Despite the decrease in the size of the aneurysms, the treatment with low-dose aspirin was continued.

Discussion

Because of its unknown etiology and pathophysiology, the diagnosis of KD is generally based on clinical features. Classic diagnostic criteria for KD consist of daily high-spiking fever for at least five days with at least four of five other principal manifestations of the illness: (1) bulbar conjunctival injection without exudate; (2) changes in the oral mucosa, including red fissured lips, red mouth and throat, and strawberry tongue; (3) redness and swelling of the hands and feet, and subsequent periungual desquamation; (4) erythematous primarily truncal rash; and (5) cervical lymphadenopathy³. Usual laboratory findings in KD patients include elevated ESR and CRP, hypoalbuminemia, elevated serum

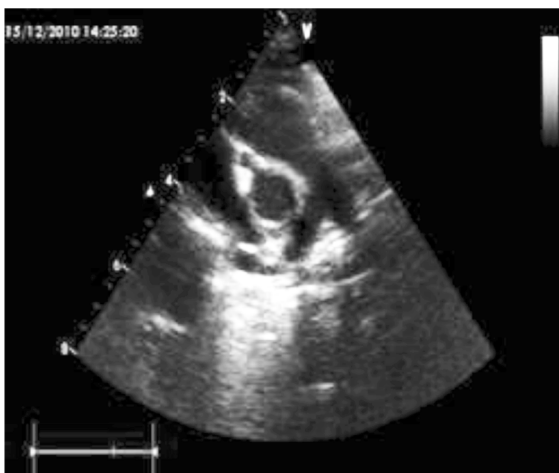


Fig. 1. Echocardiogram showing saccular aneurysm of the right coronary artery (3.5 mm in width).



Fig. 2. A fusiform aneurysm of the left coronary artery (4.5 mm in width and 8 mm in length).

hepatic transaminases, and leukocytosis, with thrombocytosis noted later in the course of the illness^{4,5}.

When patients fail to meet “classic” clinical features but have laboratory findings usually associated with KD and no reasonable alternate diagnosis, they are said to have incomplete or atypical KD^{4,5}. Incomplete KD is most common in young infants who are at the greatest risk for coronary artery disease. In the first six months of life, KD is rare, accounting for only 1.6% of all KD cases and often presenting as incomplete KD mimicking rather common exanthematic diseases of childhood. Infants have accounted for 31.2-46% of incomplete KD cases in previous studies^{1,6}.

The diagnosis of incomplete KD cases is difficult. Our case had long-lasting fever and did not satisfy any of the five other criteria, and hence, fits into incomplete KD. Other associated noncardiac features of KD may be extreme irritability, arthritis, aseptic meningitis, diarrhea, hepatic dysfunction, and hydrops of the gallbladder⁷. In our case, extreme irritability was part of the clinical picture. Laboratory features in KD are specifically related to the acute phase of inflammation. Elevated WBC with predominance of neutrophils and elevated ESR and CRP are almost universally present in the first week of illness, and may persist for four to six weeks. Notably, thrombocytosis is classically associated with KD three to four weeks after clinical onset⁷. Our child had all the above laboratory features of KD, and the laboratory findings are not different between typical and incomplete cases.

Although infants have the highest incidence of KD, it is rare in young infants ≤ 3 months of age. The annual incidence in infants ≤ 3 months of age (40.6/100,000) was much

lower than that in infants 3-11 months of age (180.4/100,000) in Taiwan⁸. In Chuang et al.’s study⁶, the percentages of incomplete form of KD and coronary artery abnormalities were 76% and 80%, respectively, in infants less than three months of age. Most of the incomplete cases fulfilled the diagnostic criteria as fever plus three criteria, while only one of the 19 incomplete cases had fever plus 0 criteria, like our patient. Moreover, Chang et al.⁹ reported that the infants less than six months of age were more likely to have incomplete presentation (35% vs. 12%), coronary involvement (65% vs. 19%), late IVIG treatment, and relatively poor outcome. In addition to the coronary involvement, the younger age group also had a higher incidence of myocardial and pericardial involvement. Fewer patients received IVIG within 10 days, and myocardial infarction was suspected more frequently in the younger age group. In our previous study, we established that incomplete KD was more common in patients younger than 1 year of age (25% vs. 12.5%), and coronary involvement was more common in incomplete cases (37.5% vs. 31.3%)¹⁰. Thus, delayed and incomplete clinical presentation could postpone IVIG treatment and cause a poor outcome.

In conclusion, the diagnosis of KD in infants is often challenging, since they are more likely to have an incomplete presentation. This can lead to a delay in the diagnosis and treatment of KD, which has been suggested to be a major contributor to the development of coronary artery abnormalities. Thus, incomplete KD should always be included in the differential diagnosis of an infant with persistent fever, especially one younger than three months of age, when the conventional work-up fails to reveal the underlying cause.

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