

Kawasaki disease shock syndrome: a severe form of Kawasaki disease

Rana İşgüder¹, Önder Doksöz², Özlem Bağ¹, Hasan Ağın¹, Timur Meşe², Ünal Utku Karaarslan¹, İlker Devrim³

Units of ¹Intensive Care, ²Cardiology, and ³Infectious Diseases, Dr. Behçet Uz Children's Research and Training Hospital, İzmir, Turkey. E-mail: dr.ranaosguder@yahoo.com

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Kawasaki disease is a systemic vasculitis, primarily encountered in children. Its clinical presentation is well known, and coronary artery abnormalities are classical complications. Shock is not a common form of presentation of the disease. We report a case who presented with shock due to Kawasaki disease in accordance with the recently defined 'Kawasaki disease shock syndrome'. In pediatric intensive care units, Kawasaki disease shock syndrome may be misdiagnosed as toxic shock syndrome. Intensivists and emergency room physicians should be aware of this uncommon presentation and perform an echocardiography to search for coronary involvement in case of clinical doubt.

Key words: Kawasaki disease, Kawasaki disease shock syndrome, toxic shock, pediatric intensive care unit.

Kawasaki disease (KD), formerly called mucocutaneous lymph node syndrome, is one of the most common vasculitic syndromes of childhood.¹ The characteristic clinical features of KD are prolonged unexplained fever for more than five days accompanied by a bilateral nonexudative conjunctivitis, erythematous rash, cervical adenopathy, oropharyngeal erythema, and swelling of the dorsa of the hands and feet.¹ Although it is typically a self-limited condition, cardiovascular complications, particularly coronary artery aneurysms, which can lead to occlusion and cardiac ischemia, may develop and cause significant morbidity and mortality.²

The Kawasaki disease shock syndrome (KD-shock syndrome) has been described recently and defined as the presence of any of the following conditions: systolic hypotension (< -2 SD blood pressure defined for age and sex), a decrease in systolic blood pressure from baseline of >20% or clinical signs of poor perfusion with accompanying features of KD.^{3,4} Although KD is a well-known and easily diagnosed syndrome, when suspected, KD-shock syndrome is a little-known and underdiagnosed type of the disease among pediatricians and intensive care practitioners.

This report describes a six-year-old girl presenting with prolonged fever and shock features. She was firstly misdiagnosed as toxic shock syndrome but was later diagnosed with KD-shock syndrome when it was considered.

Case Report

A previously healthy six-year-old girl was referred to the Pediatric Intensive Care Unit of Behçet Uz Children's Hospital with prolonged fever, fatigue and abdominal pain. On admission, she was conscious with Glasgow Coma Scale 15, heart rate (HR) 128/min, respiratory rate 20/minute, and blood pressure (BP) 56/31 mmHg. Initial cardiovascular and respiratory examination findings were normal except for tachycardia, hypotension and delayed capillary filling time. She was diagnosed with toxic shock syndrome and administered intravenous (IV) fluid 400 ml/m² initially, followed by 3000 ml/m²/24 hours and dopamine infusion. However, when evaluated after clinical stabilization, bilateral nonexudative conjunctivitis, strawberry tongue, unilateral cervical lymphadenopathies, perianal desquamation, icterus, and hepatomegaly were observed. Laboratory studies revealed

mild anemia (hemoglobin [Hb]: 9.6 g/dl) and leukocytosis (white blood cells [WBC]: 21500/mm³), but no thrombocytosis, with elevated sedimentation rate. Mild elevation of aminotransferases with indirect hyperbilirubinemia (alanine aminotransferase [ALT]: 45 U/L, aspartate aminotransferase [AST]: 60 U/L, total bilirubin 8.7 mg/dl, direct bilirubin 6.1 mg/dl), and normal coagulation profile were recorded. Cardiac panel, including creatine kinase MB (CK-MB) 2.6 mg/ml (0-4.3) and troponin I <0.05 ng/ml (0-0.4), was normal. Urine analysis revealed sterile pyuria. Bacteriological cultures of blood, throat and urine and serological tests for viruses (human immunodeficiency virus, hepatitis A, B and C virus, Epstein-Barr virus, measles and rubella) excluded a bacterial sepsis and viral infection.

She was diagnosed as KD with prolonged fever and accompanying features and diagnosed as KD-shock syndrome with hypotension and clinical signs of poor perfusion on admission. Echocardiography revealed first-degree mitral and tricuspid valve regurgitation with dilatation of the proximal left (4.6 mm) (Fig. 1) and right (4.64 mm) coronary arteries, and ejection fraction (EF) was 51%. She was administered a high dose of intravenous immunoglobulin (IVIG) (2 g/kg) and acetylsalicylic acid (80

mg/kg/d). Her fever was controlled after 24 hours of IVIG therapy. On the third day of admission, a second echocardiography showed prominent traces of the coronary artery with trivial mitral and tricuspid valve regurgitation. Repeated echocardiography in the second week of the disease showed improved systolic function (EF 62%) with normal traces of the coronary arteries (Fig. 2) and normal mitral/tricuspid valve. The patient was discharged home, clinically well, on low-dose aspirin.

Discussion

Kawasaki disease (KD) is the most common cause of acquired heart disease in the pediatric age group causing permanent damage to the coronary arteries in up to 25% of untreated children.⁵ A wide spectrum of clinical features was reported, but shock is not one of the common forms of presentation of the disease.⁶ Children with shock are usually referred to intensive care units, but KD-shock syndrome is underdiagnosed if pediatricians and intensive care units practitioners are unaware of this presentation form. Furthermore, misdiagnosis of KD may result in failure to prevent potentially life-threatening coronary artery damage.⁷

The KD-shock syndrome, firstly described by Kanegaye et al.³, is characterized by

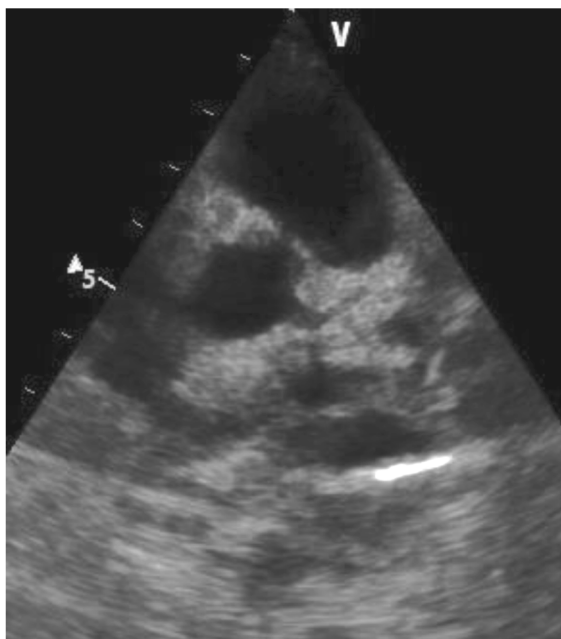


Fig. 1. Proximal left coronary artery dilatation (4.64 mm) before intravenous immunoglobulin treatment.



Fig. 2. Normal traces of the left coronary artery after intravenous immunoglobulin treatment (3.18 mm).

myocardial dysfunction, earlier onset and more severe coronary artery involvement, and poor response to standard therapy. Although children with Kawasaki disease generally do not develop a real shock¹, the differential diagnosis is required because of overlapping clinical features with toxic shock syndrome. In fact, the initial diagnosis was toxic shock syndrome in our case as well. Toxic shock syndrome is an acute exotoxin-mediated multisystem disorder caused by superantigens produced by *Staphylococcus aureus* or *Streptococcus pyogenes* infections. The diagnostic criteria of staphylococcal toxic shock syndrome include fever higher than 38.9°C, hypotension and rash with subsequent desquamation and further clinical features involving mucous membranes, central nervous system, and gastrointestinal and hematological systems⁸. Negative culture results and serological tests for bacterial and viral infections help to exclude toxic shock syndrome, while an echocardiography revealing coronary involvement confirms the diagnosis.

The similar presentations of KD-shock syndrome and toxic shock syndrome suggest that bacterial superantigens may be involved in the pathogenesis^{9,10}. It is hypothesized that the vasculitis in KD may be triggered by an immune response to a superantigen from an infectious pathogen in genetically susceptible individuals¹⁰. Matsubara et al.¹⁰ reported a skewed T-cell pool in KD patients, and animal models have demonstrated hallmarks of superantigen-mediated response. We speculate that KD-shock syndrome is probably related with an exaggerated response to superantigens, even though an infectious etiology cannot be demonstrated.

Patients with KD-shock syndrome are reported to have higher C-reactive protein levels, impaired coagulation, platelet dysfunction, and cardiac abnormalities including impaired left ventricular systolic function, mitral regurgitation, and early-onset and more severe coronary artery abnormalities compared with hemodynamically stable KD. They are also reported to show poor response to IVIG and require additional treatment for disease control³. A first-degree mitral/tricuspid valve regurgitation with systolic dysfunction and bilateral dilatation was observed in our case in addition to proximal coronary arterial dilatation.

In contrast with Kanegaye et al.'s³ report, our patient was responsive to IVIG infusion 2 g/day and did not require an additional dose of IVIG or alternative therapies.

In conclusion, KD-shock syndrome is an underdiagnosed type of KD. Pediatric intensivists and emergency room physicians should be aware of this uncommon presentation of KD and perform an echocardiography to search for coronary involvement in case of clinical doubt.

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