J Med Sci 2012;32(6):297-300
http://jms.ndmctsgh.edu.tw/3206297.pdf

Diagnosis of Atypical Kawasaki Disease Using the New American Heart Association Criteria: Reports of Two Cases and A Review of the Literature

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This study evaluated the diagnosis of atypical Kawasaki disease (KD) in accordance with the new American Heart Association (AHA) criteria. Diagnosis and treatment of this disease is always delayed in patients with prolonged fever and suspected KD, because they do not completely satisfy the traditional AHA criteria for KD. We report the cases of two patients with atypical KD. KD was successfully diagnosed in both patients by using the new AHA diagnostic algorithm, and a good response to the initial treatment with intravenous immunoglobulin was observed within 10 days of KD onset. Herein, we report these cases and review the literature.

Key words: Kawasaki disease, coronary artery lesions, immunoglobulin

INTRODUCTION

KD is an acute febrile systemic vasculitis and was first described by Kawasaki and colleagues in 1974,[1] but its cause is still unknown. In developed countries, KD is the leading cause of acquired heart diseases in children.[2,3] KD occurs worldwide and mainly affects children below 5 years of age, particularly in Asian countries, including Japan, Korea, and Taiwan; the disease has an incidence of 69–213 per 100,000 in children aged under 5 years.[4-6] The clinical characteristics of KD patients include prolonged fever for more than 5 days, diffuse mucosal inflammation, non-purulent conjunctivitis in both eyes, dysmorphous skin rashes, indurative angioedema over the hands and feet, and cervical lymphadenopathy.[7,8] In addition to the aforementioned characteristics, a broad range of nonspecific clinical characteristics such as irritability, uveitis, aseptic meningitis, cough, vomiting, diarrhea, abdominal pain, hydrops of the gallbladder, urethritis, arthralgia, arthritis, hypoalbuminemia, liver dysfunction, sensory hearing loss, and heart failure, are observed.[3,9] The most serious complication of KD is the occurrence of coronary artery lesions, including myocardial infarction, coronary artery fistula, coronary artery dilatation, and coronary artery aneurysm.[10,11]

The incidence of KD appears to be increasing.[5] However, a number of patients who have been diagnosed with KD do not satisfy the traditional American Heart Association (AHA) criteria. Technical improvements and echocardiography performed early in the course of the disease allow physicians to detect minor coronary dilation or aneurysms in patients who do not meet the traditional diagnostic criteria. In 2004, the AHA proposed a new algorithm for KD diagnosis comprising laboratory findings and echocardiographic criteria in the absence of any clinical signs of KD (Table 1). These new diagnostic criteria may alter the detection rate of KD. The new AHA criteria have been reported to be helpful for the diagnosis of KD in cases where patients did not present with all the symptoms.[12] Later AHA criteria also suggest Z score for coronary artery lesion detection. We report the cases of two patients with atypical KD who did not satisfy the classical KD criteria, who were diagnosed by the application of the new AHA diagnostic algorithm and successfully treated with intravenous immunoglobulin (IVIG) treatment within 10 days of disease onset.

Received: March 27, 2012; Revised: August 9, 2012; Accepted: September 5, 2012
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Table 1 The 2004 American Heart Association criteria for diagnosis of atypical Kawasaki disease

Criteria	Patient 1	Patient 2
(1) albumin ≤ 3.0 g/dL		√
(2) anemia for age	√	√
(3) elevation of alanine aminotransferase		√
(4) platelets after 7 days ≥ 450,000/mm^3	√	√
(5) white blood cell count ≥ 15,000/mm^3		√
(6) urine ≥ 10 white blood cells/high-power field	√	

Patients with fever for ≥ 5 days (with 2 or 3 principal clinical features for KD, C-reactive protein (CRP) ≥ 3.0 mg/dL and/or erythrocyte sedimentation rate (ESR) ≥ 40 mm/h) without other explanation should undergo laboratory testing, and if there is evidence of systemic inflammation, an echocardiogram should be obtained even if the patient does not fully meet the clinical criteria for KD. If ≥ 3 supplement criteria are met, intravenous immunoglobulin (IVIG) can be prescribed before performing echocardiography

CASE REPORTS

Patient 1

A 7-month-old boy was brought to our hospital with a 1-day history of fever accompanied by mild cough and skin rash. Physical examination revealed fever, conjunctival injection without exudates, erythematous wheal over the back and abdominal areas, erythematous indurations at the bacillus Calmette-Guerin (BCG) inoculation site, and cracked lips. The patient showed no signs of cervical lymphadenopathy or changes in his peripheral extremities. The findings of the initial laboratory tests were as follows: leukocyte count, 9,800/mm^3, with a differential cell count of 39% segmented neutrophils; lymphocytes, 49%; eosinophils, 4%; monocytes, 8%; hemoglobin (Hb) level, 8.0 g/dL (mean corpuscular volume [MCV], 63.1 FL); platelet count, 616,000/mm^3; C-reactive protein (CRP) level, 19.1 mg/L; aspartate transaminase (AST) level, 34 U/L; alanine transaminase (ALT) level[13], 22 U/L; and albumin level, 4.2 g/dL. Urinalysis revealed a white blood cell (WBC) count of 40/uL (normal range, <15/uL). Because the patient developed pyuria, we suspected he had a urinary tract infection, and therefore treated him with first-generation cephalosporin (100 mg/kg per day). No bacterial growth was detected in urine or blood cultures. The findings of follow-up laboratory studies performed on the third day after admission were as follows: leukocyte count, 9,500/mm^3, with a differential cell count of 44% segmented neutrophils; lymphocytes, 43%; eosinophils, 4%; monocytes, 9%; Hb level, 7.2 g/dL (MCV, 64.4 FL); platelet count, 589,000/mm3; C-reactive protein (CRP) level, 38.6 mg/L; AST level, 28 U/L; ALT level, 15 U/L; and albumin level, 3.5 g/dL. Fever persisted, and two-dimensional (2D) echocardiography was performed on the fifth day following admission under suspicion of atypical KD (using the new AHA diagnostic algorithm). Echocardiography revealed dilatation of the right coronary artery (RCA; 3.09 mm). The patient was administered IVIG (2 g/kg per day) for 12 h. Fever subsided within 24 h following IVIG treatment and administration of a low dose of aspirin (3–5 mg/kg per day). The patient was discharged on the eighth day of admission; desquamation over his finger tips was observed on the fourth day after discharge. Follow-up echocardiography performed 8 months after discharge revealed resolution of RCA dilatation (RCA diameter, 2.3 mm). Follow-up examination performed 6 months later revealed an Hb level of 12.1 g/dL (MCV, 75.7 FL); further, no signs of thalassemia were detected on electrophoresis. Pyuria, anemia, and platelet counts satisfied the criteria of the new diagnostic AHA algorithm.

Patient 2

A 3-year-old boy was brought to our hospital with a 3-day history of fever and cervical lymphadenopathy. The patient showed no signs of conjunctival injection or skin rash, or changes in lips, oral cavity, and peripheral extremities. The findings of the initial laboratory studies were as follows: leukocyte count, 18,700/mm^3, with a differential cell count of 85% segmented neutrophils; lymphocytes, 9%; monocytes, 5%; Hb level, 12.2 g/dL (MCV, 88.5 FL); platelet count, 295,000/mm^3; CRP level, 127.4 mg/L; AST level, 173 U/L; and ALT level, 111 U/L. Computed tomography of the neck and head showed acute left tonsillitis with lymphadenopathy on both sides of the neck. The patient was prescribed amoxicillin/clavulanate and aminoglycoside for 5 days for the management of lymphadenopathy; however, fever persisted. The findings of follow-up laboratory studies performed on the fourth day of admission were as follows: leukocyte count, 18,300/mm^3, with a differential cell count of 72% segmented neutrophils; lymphocytes, 15%; monocytes, 12.5%; Hb level, 10.7 g/dL (MCV, 89.2 FL); platelet count, 307,000/mm^3; and CRP level, 220.6 mg/L. Therapy was switched to teicoplanin and third-generation cephalosporin on the fifth day after admission. Conjunctival injection without exudation and cracked lips were observed on the seventh day; moreover, fever persisted. The findings of follow-up laboratory tests performed on the eighth day of admission were as follows: leukocyte count, 15,200/mm^3, with a differential cell count of 68%

segmented neutrophils; lymphocytes, 18%; monocytes, 11%; Hb level, 10.5 g/dL (MCV, 89.9 FL); platelet count, 541,000/mm^3; CRP level, 138.0 mg/L, albumin level, 2.7 g/dL; AST level, 32 U/L; ALT level, 27 U/L; and urinalysis WBC count, 0/uL. Two-dimensional echocardiography performed under the suspicion of atypical KD (diagnosed according to the new AHA algorithm) revealed dilatation of the left coronary artery (LCA, 3.85 mm). IVIG (2 g/kg per day) was administered for 12 h on the eighth day of admission. Fever subsided within 24 h of IVIG treatment. The patient was discharged on the twelfth day after admission. Follow-up echocardiography performed 2 months later revealed resolution of LCA dilatation (diameter, 2.4 mm). Total leukocyte count, Hb level, platelet count, liver enzyme levels, and albumin level satisfied the new AHA criteria.

DISCUSSION

The incidence of KD was found to have increased, and this observation might be attributed to the new and better methodology for KD detection. However, recent retrospective studies seem to confirm that the incidence is higher than previously reported. This increased incidence of KD may also be attributed to better identification of patients with incomplete presentation of the disease. Atypical or incomplete KD frequently leads to delays in diagnosis and treatment. Delayed diagnosis is associated with increased risk of coronary artery aneurysms, but not with patients showing a delay in seeking medical consultation.[14] In our previous study, incomplete cases accounted for 15% of confirmed cases of KD.[2]

The 2004 AHA criteria[13] for the diagnosis of atypical KD included 2 main criteria of an erythrocyte sedimentation rate (ESR) ≥ 40 mm/h and a CRP level ≥3.0 mg/dL, or both, in addition to at least 3 supplemental laboratory criteria (albumin level ≤ 3.0 g/dL; anemia for age; elevated ALT levels; platelet count after 7 days ≥450,000/mm^3; WBC count ≥15,000/mm^3; and ≥10 white blood cells per high-power field in urine samples). Heuclin and colleagues have reported that the detection rate of KD in Europe increased after the introduction of the new diagnostic algorithm, which included early use of echocardiography. The new AHA diagnostic algorithm (laboratory tests and early echocardiography) was clearly helpful for the diagnosis of atypical KD.[12]

Herein, we reported two cases of atypical KD that were successfully diagnosed and treated within 10 days of illness. We also recommend that laboratory tests for atypical KD according to the new AHA algorithm should be conducted for any unexplained fever in children that persists for more than 7 days; these should include assessments of albumin level, Hb level, alanine aminotransferase level, platelet counts, white blood cell count, and urinalysis.

DISCLOSURE

All authors declare that this study has no conflict of interest.

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