Introduction

The etiology of Kawasaki disease (KD) is still unknown and no single pathognomonic clinical or laboratory finding for its definitive diagnosis has been identified. To establish a diagnosis, we inevitably depend on the diagnostic criteria that include the typical constellation of symptoms and signs noted by the Japanese Kawasaki Disease Research Committee or by the American Heart Association (AHA). However, pediatricians occasionally encounter febrile children who do not fulfill the diagnostic criteria but who have several findings compatible with those of KD. In this type of situation, the diagnosis of incomplete KD is a clinical challenge that cannot be avoided by delaying the diagnosis because the risk of coronary complications is seen even in incomplete presentation of the disease.

Since 1966, the Korean Pediatric Society has recommended that a routine universal Bacille Calmette-Guérin (BCG) vaccination be given to neonates. In Korea, nearly all neonates receive the BCG vaccine by one month of age. Erythema, induration, or crust at the BCG inoculation site (BCGitis) is listed as a significant finding among the diagnostic guidelines for KD by the Kawasaki Disease Research Committee in Japan and by the AHA. Recently, BCGitis was reported to be a useful diagnostic tool for identifying incomplete KD in several cases. We have considered BCGitis as a pathognomonic finding of KD, and have applied it to the diagnosis of KD in infants, as BCGitis was reported to have been observed in more than 50% of...
KD patients 1 to 12 months following BCG inoculation. Our study was designed to test how the BCGitis can be a diagnostic feature of KD by comparing patients with complete disease presentation and those in whom incomplete KD was diagnosed based on a BCGitis.

Subjects and Methods

Study population

From January 2006 to February 2012, 490 patients with KD were admitted to Asan Medical Center in Seoul, Korea. Of these patients, 101 were less than 12 months of age at the time of admission. Sixty-seven patients met the AHA diagnostic criteria of KD. Fifty-four patients showed BCGitis during the acute phase of illness, and were assigned to the complete presentation group. Of the remaining 34, 29 patients showed BCGitis during the acute phase of illness, and were assorted to the incomplete presentation group. All 83 enrolled patients had been inoculated with BCG during the neonatal period. If a patient had been examined initially by a clinically experienced pediatrician, a fever of 3 or 4 days’ duration was permitted to establish a diagnosis. As controls for evaluating the diameters of coronary arteries, we enrolled 31 healthy infants, who had been referred to Asan Medical Center for evaluation of a cardiac murmur during the past year and for whom the clinical and echocardiographic examinations showed no evidence of cardiac disease.

The Institutional Review Board of the Medical Center approved this retrospective study (2012-0011) and waived the need for patient consent. Demographic, laboratory, and clinical data were obtained from patients’ medical records.

Echocardiographic data

Echocardiographic examinations were performed 3 times using a Vivid 7 Vantage machine (GE Vingmed, Horten, Norway), i.e., during the acute phase, the subacute phase (a subsiding of fever 4 weeks after the onset of disease), and the convalescent phase (4-12 weeks after the onset of disease). Stored echocardiographic images were reviewed by one author who was blinded to patient status. The following diameters were measured by EchoPAC PC, Version 7 (GE Vingmed, Horten, Norway) using the method of de Zorzi et al. of the left main coronary artery (LMCA), the left anterior descending artery (LAD), and the right coronary artery (RCA).

We randomly selected 19 images of coronary arteries to determine the intra- and inter-observer variability in the measurement of the coronary artery diameters. The intra-observer percent precision in diameter measurement of LMCA, LAD, and RCA were 5.4%, 8.7%, and 5.1%, respectively, and the inter-observers percent precisions were 5.8%, 10.4%, and 7.0%, respectively.

The diameters of the coronary arteries were converted to a z score using the regression equations from the study of Olivieri et al.

Application of the American Heart Association algorithm for diagnosing incomplete Kawasaki disease

The AHA recommended an algorithm that included laboratory and echocardiographic criteria for the diagnosis of incomplete KD. The laboratory criteria include albumin ≤ 3 g/dL, anemia for age, elevation of alanine aminotransferase, platelets after 7 days ≥ 450000/mm³, white blood cell count ≥ 15000/mm³, and urine ≥ 10 white blood cells/ high-power field. An echocardiogram is considered positive for the purposes of this algorithm if any of 3 conditions had been met, i.e., a z-score of LAD or RCA ≥ 2.5, coronary arteries meet the Japanese Ministry of Health criteria for aneurysms, or ≥ 3 other suggestive features exist, including perivascular brightness, lack of tapering, reduced left ventricular function, mitral regurgitation, pericardial effusion, and a z score of LAD or RCA of 2-2.5. We applied this algorithm to 29 patients that had an incomplete presentation of BCGitis. However, in our clinical practice, we do not use 2 variables of the echocardiographic criteria, i.e., perivascular brightness and lack of tapering, as we consider that the former is inappropriate and the latter is too subjective. Therefore, we did not perform an investigation of these 2 variables.

Statistical analysis

All the data are presented as medians (range). All statistical analyses were performed using SAS Version 9.1 (SAS Institute, Cary, NC, USA), and statistical significance was defined as a p < 0.05. Categorical variables were compared using Fisher’s exact test. Comparisons of numerical variables between groups were performed using the Wilcoxon rank sum test.

Results

The clinical and laboratory findings of patients with KD are presented in Table 1. The frequencies of the classic, principal diagnostic features in the incomplete presentation group were appropriately lower than those in the complete presentation group. The less frequently appearing features included cervical lymphadenopathy (3.4%) and palmar erythema (20.7%) in the incomplete presentation group. No other clinical or laboratory findings differed between the 2 groups. In the incomplete presentation group, there were 17 (58.6%) patients with 3 principal features, 8 (27.6%) with 2 principal features, and 4 (14.0%) with 1 principal feature. In the control subjects, the median age was 7.2 months (p = 0.8663 compared to the complete presentation group, and p = 0.1524 compared to the incomplete presentation group), and there were 14 (45.2%) females (p =
Echocardiographic features were compared between the patient groups and the controls (Table 2) (Fig. 1). The systolic function variables and the frequencies of mitral regurgitation and pericardial effusion did not differ between the patient groups. The z scores of the LMCA diameters (p=0.0192 in the complete presentation group and p=0.0022 in the incomplete presentation group during the acute phase, p=0.0073 and p=0.0234, respectively, during the subacute phase and p=0.0290, respectively, during the convalescent phase) and the RCA (p<0.0001 and p<0.0001, respectively, during the acute phase, p=0.0003 and p<0.0001, respectively, during the subacute phase, and p=0.0104, respectively, during the convalescent phase) of the patients were consistently greater than those of the controls throughout the 3 phases of illness. The LAD (p=0.0014 and p=0.0023, respectively, during the acute phase, and p=0.0085 and p=0.0317, respectively, during the subacute phase) of the patients were also greater than those of the controls, although they (p=0.2209 and p=0.0617, respectively) were not significantly greater during the convalescent phase. The z scores of the diameters of coronary arteries did not differ between the 2 patient groups. Only the z score of RCA in the incomplete group (p=0.0447) was greater than that of the complete group during the subacute phase. Comparisons of the diameters of coronary artery between groups showed a similar pattern.

We divided the incomplete presentation group into subgroups with 3 and with <3 classic diagnostic principal features. We compared all of the variables presented in Table 1 and 2 between the subgroups; however, we could not find any variables showing a significant difference between the subgroups. Additionally we compared all of the variables between the complete presentation group and 13 excluded patients with complete presentation who did not have BCGitis, we could not find any variables showing a significant difference. These results are not presented in this paper.

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We applied the AHA algorithm for diagnosis of incomplete KD to 29 patients in the incomplete presentation group. The results are summarized in Fig. 2. Two patients were not eligible for use of the AHA algorithm.21 Incomplete KD could be diagnosed in 5 (18.5%) of the 27 patients, i.e., 2 (7.4%) based on laboratory criteria and 3 based on echocardiographic criteria. In 15 patients (55.6%), a diagnosis of incomplete KD was not possible; 12 patients did not fulfill the laboratory and echocardiographic criteria, and in 3 patients, the values of acute-phase reactants were less than the threshold 0.1533 and p=0.7997, respectively).

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value. In 7 patients, the diagnosis was inconclusive because of the absence of data regarding 2 echocardiographic variables.

**Discussion**

When the clinical, laboratory, and echocardiographic variables of patients with incomplete KD were compared with those of patients with complete disease presentation, there were no significant differences between the 2 groups. In addition, the z scores of coronary arteries in patients with incomplete presentation were significantly greater than those of the controls throughout the three phases of illness. The z score of LAD during the convalescent phase was an exception. In this study, the 2 patient groups differed only in the frequencies of the principal features of disease.

Sudo et al.\(^{14}\) collected data from a total of 23263 patients with KD in a nationwide survey of Japan from 2007 through 2008. In the study, incomplete KD was defined as the presence of ≤4 principal symptoms defined according to the Japanese diagnostic criteria\(^1\) (corresponding to ≤3 principal features of the AHA diagnostic criteria\(^2\)) regardless of whether the patient had coronary artery abnormalities; their incomplete presentation group included 271 children (1.2%) with only one or 2 principal symptoms.\(^{14}\) Currently, a diagnosis of incomplete KD might be performed in cases with fewer classical diagnostic criteria and several compatible clinical, laboratory, or echocardiographic findings, based on the exclusion of another febrile illness.\(^{15}\) The above-mentioned results of the survey by Sudo et al.\(^{14}\) seem to reflect the current diagnosing practice for incomplete KD. To date, there have been 2 guidelines for the diagnosis of incomplete KD. According to the Japanese diagnostic criteria,\(^1\) a diagnosis of incomplete KD is possible in a case with 4 principal symptoms and a coronary artery aneurysm. However, many authors believe that this definition is too restrictive and specific.\(^{16}\) Pediatric clinicians frequently encounter KD in suspicious cases with <4 principal symptoms. In addition, a coronary artery abnormality included

| Table 2. Echocardiographic features of Kawasaki disease patients with BCGitis by the type of presentation |
|---------------------------------------------------------------|
| **Complete KD (n=54)** | **Incomplete KD (n=29)** | **Controls (n=31)** |
| LVEDD (mm) | 24.8 (16.6 - 31.8) | 24.3 (18.2 - 29.3) | 24.1 (21.6 - 29.4) |
| FS (%) | 38.2 (24.1 - 74.0) | 36.9 (30.0 - 64.7) | 36.2 (27.0 - 51.8) |
| Mitral regurgitation (%) | 16 (29.6) | 11 (37.9) | 15 (9.1) |
| Pericardial effusion (%) | 4 (7.4) | 4 (13.8) | 2 (3.3) |

**Acute phase**

| Variable | Type | Complete KD (n=54) | Incomplete KD (n=29) | Controls (n=31) |
|----------|------|-------------------|---------------------|----------------|
| LMCA Diameter (mm) | 1.96 (1.20 - 2.90) | 2.00 (1.20 - 3.00) | 1.49 (1.00 - 2.22) |
| Z-score | 0.16 (-2.76 - 2.68) | 0.41 (-3.14 - 3.08) | -0.66 (-2.11 - 0.71) |
| LAD Diameter (mm) | 1.60 (1.00 - 2.30) | 1.60 (1.00 - 3.50) | 1.47 (1.08 - 2.77) |
| Z-score | 0.20 (-2.77 - 2.33) | 0.42 (-2.61 - 5.23) | -0.48 (-2.79 - 2.72) |
| RCA Diameter (mm) | 1.58 (0.80 - 3.20) | 1.60 (0.90 - 2.63) | 1.26 (0.82 - 1.65) |
| Z-score | -0.15 (-3.61 - 3.03) | -0.16 (-2.47 - 2.63) | -1.17 (-3.84 - 0.0) |

**Subacute phase**

| Variable | Type | Complete KD (n=54) | Incomplete KD (n=29) | Controls (n=31) |
|----------|------|-------------------|---------------------|----------------|
| LMCA Diameter (mm) | 2.00 (1.14 - 3.39) | 1.84 (1.40 - 3.20) | 1.49 (1.00 - 2.22) |
| Z-score | 0.11 (-3.10 - 3.31) | -0.02 (-1.56 - 3.35) | -0.66 (-2.11 - 0.71) |
| LAD Diameter (mm) | 1.60 (0.80 - 2.64) | 1.51 (0.90 - 3.19) | 1.47 (1.08 - 2.77) |
| Z-score | 0.03 (-3.42 - 3.17) | 0.09 (-2.76 - 3.86) | -0.48 (-2.79 - 2.72) |
| RCA Diameter (mm) | 1.50 (0.97 - 3.11) | 1.57 (1.20 - 3.02) | 1.26 (0.82 - 1.65) |
| Z-score | -0.43 (-2.52 - 3.30) | -0.25 (-1.28 - 2.85) | -1.17 (-3.84 - 0.0) |

**Convalescent phase**

| Variable | Type | Complete KD (n=54) | Incomplete KD (n=29) | Controls (n=31) |
|----------|------|-------------------|---------------------|----------------|
| LMCA Diameter (mm) | 1.99 (1.35 - 2.69) | 2.00 (1.40 - 2.65) | 1.49 (1.00 - 2.22) |
| Z-score | 0.11 (-2.23 - 1.83) | 0.10 (-1.61 - 2.11) | -0.66 (-2.11 - 0.71) |
| LAD Diameter (mm) | 1.50 (0.70 - 2.35) | 1.59 (0.80 - 2.40) | 1.47 (1.08 - 2.77) |
| Z-score | -0.15 (-3.17 - 2.30) | 0.13 (-3.48 - 2.22) | -0.48 (-2.79 - 2.72) |
| RCA Diameter (mm) | 1.49 (1.01 - 2.73) | 1.47 (0.83 - 2.34) | 1.26 (0.82 - 1.65) |
| Z-score | -0.75 (-2.59 - 2.55) | -0.63 (-3.25 - 1.52) | -1.17 (-3.84 - 0.0) |

Data are medians (range) or numbers of frequency (%). *p<0.05, group 1 vs. group 2, †p<0.05, group 1 vs. controls, ‡p<0.05, group 2 vs. controls. KD: Kawasaki disease, LVEDD: left ventricle end-diastolic dimension, FS: fraction shortening, LMCA: left main coronary artery, LAD: left anterior descending coronary artery, RCA: right coronary artery, BCGitis: Bacille Calmette-Guérin inoculation site.

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AHA proposed a diagnostic algorithm of incomplete KD in 2004, details of which were presented in the Methods section. Newburger et al. acknowledged this algorithm as only an informed opinion of a Committee of Experts (evidence level C). Although Yellen et al. tested the performance of the AHA diagnostic criteria and reported its 97% applicability, their study subjects were restricted to cases with coronary artery aneurysm. This study was the first attempt to test the performance of this algorithm in the diagnosis of incomplete KD in infants. It is well known that the incidence of incomplete presentation is relatively higher in younger patients and that there is a risk of delayed diagnosis and management in infants with incomplete presentation. In this study, 5 (18.5%) of the 27 patients with incomplete presentation that was eligible for AHA algorithm application could be diagnosed, and the laboratory criteria was only fulfilled in 3 (7.4%) patients. This disappointing result is inconsistent with the result reported by Yellen et al. In their study, the laboratory criteria were fulfilled in all patients with incomplete KD. This difference may have been caused by the differences in subjects. In the report by Yellen et al. patients who had coronary artery aneurysms were selected as subjects and the median duration of fever in the incomplete presentation group was 9 days, which seems to be longer than the 5 days encountered in our study. A high prevalence of BCGitis in KD patients who visited a hospital between 1 and 4 days after the onset of illness was reported. BCGitis has been considered to be an early manifestation of KD. To avoid coronary complications, we can use BCGitis as a specific finding in early diagnosis of incomplete KD.

The less frequently appearing classical principal features of incomplete KD have been reported to be cervical lymphadenopathy (19-38.6%) and changes in extremity (21-44.3%). These patterns and frequencies were also identified in our study and are similar to those seen in patients with complete presentation. Uehara et al. reported that redness or crust formation at the BCGitis was ob-

![Fig. 1. Z-scores of the diameters of coronary arteries (left main coronary artery in A, left anterior descending artery in B, and right coronary artery in C) during 3 phases of illness. *p<0.05, complete presentation group vs. incomplete presentation group, †p<0.05, complete presentation group vs. controls, ‡p<0.05, incomplete presentation group vs. controls.](image-url)
The z scores for the coronary artery diameters in controls may be the result of a racial difference in this study and it could be causatively associated with the low performance of the application of AHA echocardiographic criteria in the diagnosis of incomplete KD.

In summary, clinical, laboratory, and echocardiographic variables of patients with incomplete KD and BCGitis, did not differ from those of patients with complete presentation. The z scores of their coronary artery diameters were significantly greater than those of the controls. BCGitis is a robust and useful feature in the diagnosis of incomplete KD in infants who have received BCG vaccine during their neonatal period.

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