Differences over 10 years in epidemiologic and clinical features of Kawasaki disease at a single tertiary center

To the Editor.

Kawasaki disease (KD) is an acute systemic vasculitis of unknown etiology that affects infants and young children; approximately 80% of those affected are under the age of 5 years.1,2) The epidemiology of KD shows typical characteristics regarding race (northeastern Asian children, including those in Japan, South Korea, and Taiwan, have a 10-20 times higher incidence than Caucasian children), sex (boys have a 1.3-1.5 times higher incidence than girls), age (about 80% are under the age of 5 years), presence of siblings (the relative risk in siblings is 10 times higher), and seasonal incidence (peaks in winter and summer) and it usually presents as outbreaks (in Japan).3,4) These epidemiological features and the current consensus in the scientific field suggest that the pathogenesis of KD is likely to be an abnormal immune response caused by an infectious trigger that develops in genetically predisposed children.1)

We researched the incidence, treatments and coronary complications of KD in Keimyung University Dongsan Hospital in Daegu, Korea, between January 2009 and December 2018, and evaluated its differences over 10 years. This study was approved by the institutional review board of the Keimyung University Dongsan Medical Center (approval number: 2019-07-047).

A total 593 patients (357 males and 236 females) with KD were enrolled. The annual incidence of KD per 1,000 total admission patients has significantly increased over 10 years
The total number of KD has increased both for complete and incomplete KD over 10 years (standardization coefficient ($\beta$)=0.784, $R^2=0.615$, $P=0.007$ for complete KD and standardization coefficient ($\beta$)=0.904, $R^2=0.818$, $P<0.001$ for incomplete KD) (Figure 1).

In 16 patients (2.7%), the fever and clinical signs spontaneously resolved after admission without treatment, and the rest (577 patients, 97.3%) were all treated with IVIG 2 g/kg as primary IVIG therapy (Table 1). The non-responder rate to primary IVIG therapy was 24.6% (142 patients); second IVIG therapy was provided in 104 patients, intravenous methylprednisolone pulse therapy (30 mg/kg) in 35, and oral prednisolone (2 mg/kg) in 3 as the second treatment regimen. For the third treatment, 16 non-responders after the second repeat dose of IVIG received methylprednisolone pulse therapy and one patient who was a non-responder to methylprednisolone pulse therapy received infliximab. During the fourth treatment, one patient, who was a non-responder to methylprednisolone pulse therapy from the third round, received infliximab. Among 593 patients, CAD was detected in 103 patients (17.5%) and giant coronary aneurysm in 4 (0.7%). During this study period, the incidence of non-responders to IVIG and CAD showed a decrease trend over 10 years, although it was not statistical significant (standardization coefficient ($\beta$)=0.249, $R^2=0.055$, $P=0.488$ for non-responders to IVIG and standardization coefficient ($\beta$)=0.257, $R^2=0.051$, $P=0.473$ for CAD) (Figure 1).

According to a recent nationwide survey of KD, the incidence of KD significantly increased annually in South Korea (194.7-217.2/100,000 children <5 years of age in 2014) and also in Japan (308/100,000 children <5 years of age in 2014).\textsuperscript{5,6} Similarly, the incidence of KD in our study, especially incomplete KD, showed annually an increasing trend. The increasing incidence of incomplete KD may be due to the use of the systemic diagnostic algorithm for
diagnosing incomplete KD (from American Heart Association guidelines) as it helps clinicians easily diagnose incomplete KD. The treatment sequence of acute KD was well established: generally, it is IVIG as first treatment, second repeat dose of IVIG as second treatment, steroids as third treatment, and infliximab as fourth treatment. The treatment sequence of KD in our study showed a similar pattern. The overall response rate for first IVIG treatment in South Korea was 88.2%, which was little higher than in Japan (71.6-83.0%) and in US (83.7%). In our study, the response rate for first IVIG was 75.4%, and it was somewhat lower than the nationwide survey of South Korea. And the incidence of non-responders to IVIG showed a decreasing trend over time. The coronary artery dilatation occurred more often in our study than in the nationwide survey (17.5% vs 10.8%), but the coronary aneurysm occurred less in our study than the nationwide survey (0.7% vs 1.7%). As in previous studies, the incidence of CAD was showing a decreasing trend over time.

Our study has some limitations. We analyzed data through medical records retrospectively, in a single local hospital in Korea. There might be some differences in the results due to regional policies and individual preferences in the management of patients.

In conclusion, the incidence of KD, especially incomplete KD, presented an increasing trend and the incidence of non-responders to IVIG and CAD presented a decreasing trend over 10 years in our institution. At each institution, it is essential to create awareness of the importance of the epidemiological factors and the clinical features of KD in the proper and timely management of patients and the prevention of coronary complications.

References


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Conflicts of Interest
The authors declare that they have no conflicts of interest with respect to this work.
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Data are presented as total number (period 1/period 2)
Figure legends

Fig 1. The annual incidence of (1) complete and incomplete Kawasaki disease and (2) non-responders to IVIG during the study period.
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