Editorial:

Recent research trends on Kawasaki disease related to infection

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Key message
There are reports that the incidence of Kawasaki disease has decreased since the reinforcement of quarantine, and studies have reported that multisystem inflammatory syndrome in children has occurred more in areas where coronavirus disease 2019 was prevalent than in previous years. As in these studies, research trends on the etiology studies of childhood and adolescent systemic vasculitis in infection-related immune responses after the COVID-19 pandemic are becoming more active.

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Editorial:

Kawasaki disease (KD) was first described in a 1967 report by Japanese pediatrician Tomisaku Kawasaki. It is a medium-sized vessel vasculitis of undetermined etiology, usually affecting children under five years. The leading theory for the pathogenesis of KD is that an unknown infectious agent leads to the activation of the immune system in a genetically susceptible child.

In South Korea, a nationwide survey has been conducted every three years since 1994 using KD patient data. In the recent study, they noted new findings on the seasonal occurrence of KD. KD occurred most commonly in the cold winter season (December–January), as shown in most epidemiologic studies from countries with four discrete seasons. Compared with the previous surveys, the second seasonal peak of KD occurrence in South Korea moved from summer (June, July, and August) to late spring (May and June). Changes in the seasonal distribution of KD can provide potential clues about the causes of KD related to climate change and seasonal epidemics.

Various types of bacteria and viruses have been reported as infectious pathogens related to KD, and several analyses of these reports continue. Also, the geographic patterns of KD occurrence, wherein the incidence rates of KD in Northeast Asian countries, including Japan, South Korea, China, and Taiwan, are 10~30 times higher than in the United States and Europe. Differences in the seasonal incidence of KD outbreaks reported in previous epidemiological studies suggest that seasonal infections may cause specific immunological responses in the genetically vulnerable patient. Previous studies have also supported that KD is an essential mechanism by which abnormal immune responses after infection work in individuals with specific genetic backgrounds.

There are various research aspects of KD, including clinical, epidemiological, and pathophysiological aspects, but the relationship between KD and pathological infection is one of the most notable research topics. Another aspect that supports the association with infection is the significant characteristic overlap of clinical symptoms between KD and other infectious substances, particularly scarlet fever, newly described multisystem inflammatory syndrome (MIS), and adenovirus infection.

Since 2019, the coronavirus disease 2019 (COVID-19) has spread worldwide and become a global pandemic. In 2020, KD-like illness was reported in children’s patients infected with COVID-19 for the first time in Europe, which has alarmed pediatricians. It has currently reported in many countries around the world. Severe MIS in children (MIS-C) has been
reported in children under 19 years with active or recent infections of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).\(^5\)\(^-\)\(^7\) So far, SARS-CoV-2 is poorly understood pediatric systemic vasculitis.

After the COVID-19 pandemic in Bergamo province of Italy, a 30-fold increase in the incidence of KD-like illness compared to the last five years has been described. Also, recent reports indicate that the number of KD-like illness has significantly increased compared with that in previous years in the United States, Italy, and the United Kingdom, where COVID-19 was more prevalent, raising expectations that confirm the association between KD and infections.\(^8\)

Compared to that, recent reports showed that the incidence of KD significantly decreased when compared with that in the same previous period during the COVID-19 pandemic, when implemented “mask-wearing” and “social distancing”. The decrease in the incidence of KD is estimated to have been affected by the prevention of general virus infections through strengthening quarantine measures, which are the results of supporting that infection is related to KD disease.\(^9\),\(^10\)

MIS in children (MIS-C) has features that overlap with myocarditis, toxic-shock syndrome and KD. Especially, MIS-C may show signs and symptoms similar to KD, but there are also several differences. MIS-C is more common in older children than KD, and the most frequent clinical characteristics are gastrointestinal or neurological symptoms. MIS-C often presents with shock, making it difficult to regard it as the same disease. Therefore, epidemiological, clinical and immunological differences distinct from KD.

Based on the COVID-19 pandemic situation, current research trends on KD should further study and analyze similarities and differences between KD and MIS pathogenesis and focus on etiology studies of childhood and adolescent systemic vasculitis in infection-related immune responses.


