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EDITORIAL COMMENTARY

Kawasaki Disease and Infections: A Myth or a Reality?

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Kawasaki disease (KD) is an acute systemic small- and medium-vessel vasculitis of childhood with a potential to cause serious cardiac morbidity [1]. The standard of care is intravenous immunoglobulin, which decreases the risk of coronary artery lesions from 25% to 4%–5% [1]. However, etiology of KD still remains an enigma [2]. Infections, environmental factors, and genetic predisposition have been implicated. Association of COVID-19 with multisystemic inflammatory syndrome in children (MIS-C), which has overlapping clinical features with KD, has revived interest of the scientific community to solve this enigma [2].

An infectious etiology of KD was suggested due to marked seasonality, geographical clustering, predisposition in under-fives, and overlapping clinical features [1, 2]. Various bacterial, viral, and parasitic infections have been described in association with KD. Superantigen-mediated immune response has been implicated because of similarities in the clinical and immunological profiles of KD and toxic shock syndrome. However, no infectious agent has been proven to be consistently associated with KD.

In this issue of the Journal, Mahajan et al. have described KD in close temporal association with viral and bacterial infections [3]. Several case reports have also described simultaneous occurrence of infection and KD [4, 5].

In contrast, epidemiological studies point to longer intervals between infection and KD. Kang et al. observed outbreaks of KD 1–3 mo after the outbreaks of varicella and respiratory viral infections in a large cohort in South Korea [6]. Reduction in incidence of KD was observed in South Korea after introduction of nonpharmaceutical interventions to reduce spread of COVID-19, thus implicating infections as probable triggers for KD [6]. Hara et al. documented more impressive reduction in droplet- and contact-transmitted infections (75%) than in KD (27%) during COVID-19 pandemic, thus excluding the role of droplet and contact transmission in development of KD in Japan [7].

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In another population-based study from Taiwan, Weng et al. observed 56% higher cumulative incidence of KD in enterovirus-infected cohort as compared to nonenterovirus-infected cohort and this risk persisted over a follow-up period of nearly 8 y [8]. They excluded all children who developed KD at the time of diagnosis of enterovirus infection in this series. Such long intervals between infection and KD make the task of implicating infections as a direct cause of KD even more difficult. In summary, though the epidemiologic studies point to an infectious etiology of KD, no infectious agent has been consistently associated with it [9]. An abnormal immune response triggered by an infectious agent in a genetically predisposed host seems to be the most likely mechanism of KD [2].

In Mahajan's series, persistence or re-emergence of fever along with other clinical features consistent with KD led to a diagnosis of KD. Diagnosis of KD should be made with caution in a child with proven infection because of the overlapping clinical and laboratory features. In a setting of immune activation, serological positivity for infections should be interpreted carefully. Incidence of coronary artery lesions was very high (80%) in Mahajan's cohort. Since the data were collected from January 2019 to January 2021, some of the patients in this series might have had MIS-C in association with COVID-19 infection. While timely diagnosis and treatment of KD prevents coronary involvement, it is imperative not to overdiagnose KD; and physicians should be aware of other etiologies of persistent or recurrent fever in a setting of proven infection.

Declarations

Conflict of Interest None.

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