Could the increasing concerns regarding the post-COVID-19 symptoms cause Kawasaki disease to be under-diagnosed?

Sirs,

We read the article "Severe refractory Kawasaki disease in seven infants in the COVID-19 era" with a great interest (1). In the described cohort, 7 infants were diagnosed as Kawasaki disease (KD), all of them were intravenous immunoglobulin (IVIG) non-responders and required further biological treatment. Two patients were tested positive for Coronavirus disease 2019 (COVID-19).

Previous data suggested that children are not vulnerable to COVID-19 as much as adults (2). However, children with hyperinflammation resembling KD, related to COVID 19 and associated with poor prognosis were recently reported (3, 4). Although concerns regarding the possible link between COVID-19 and KD are raised, as demonstrated by Ouldali *et al*. (5) who reported the increased incidence of KD in the current pandemic era compared to the pre-pandemic period, we have not observed the same situation in our tertiary paediatric rheumatology centre. However, we have observed that some Kawasaki patients were resistant to conventional treatments and presented unusual features (*e.g*. more severe cardiac involvement and gastrointestinal symptoms).

Thus, we would like to present a severe form of infantile KD. A five-month-old girl admitted to emergency unit due to fever lasting for 1 day. Her initial physical examinations and laboratory evaluation were unremarkable. A non-specific viral infection was considered, and symptomatic medication was prescribed. A few days later, rashes and bilateral non-purulent conjunctivitis were added, pyuria was detected, transaminases and C-reactive protein were increased. She was considered to have urinary infection and allergic rashes. Antibiotic and antihistaminic treatments were started. Although there was no contact history of the patient and her household members, serological and polymerase chain reaction tests for COVID-19 were performed to the patient which resulted to be negative. Echocardiographic, abdominal and urinary ultrasonographic screenings were normal. The diagnosis of sepsis was considered and IVIG (0.8 gr/kg/dose) was given. On the 25th day of the disease, the patient was referred to our department. High fever with remitting pattern persisted. She had extensive rashes, unilateral cervical lymphadenopathy, oedema on back of her hands, arthritis of her ankles and wrists, fissured lips and conjunctivitis. Thrombocyte count was elevated (743,000/mm^3). The definite diagnosis of KD was established. IVIG was administered at a dose of 2 gr/kg. As a long-term treatment, 2 mg/kg/day methylprednisolone and 3 mg/kg/day acetylsalicylic acid were added. Three days later, all of the symptoms recovered. However, in the control echocardiographic evaluation, multiple giant coronary aneurysms were observed (Fig. 1). Infliximab at a dose of 5 mg/kg was introduced and enoxaparin was added. Although not at the desired level, a regression of aneurysms was noted in her subsequent follow-ups.

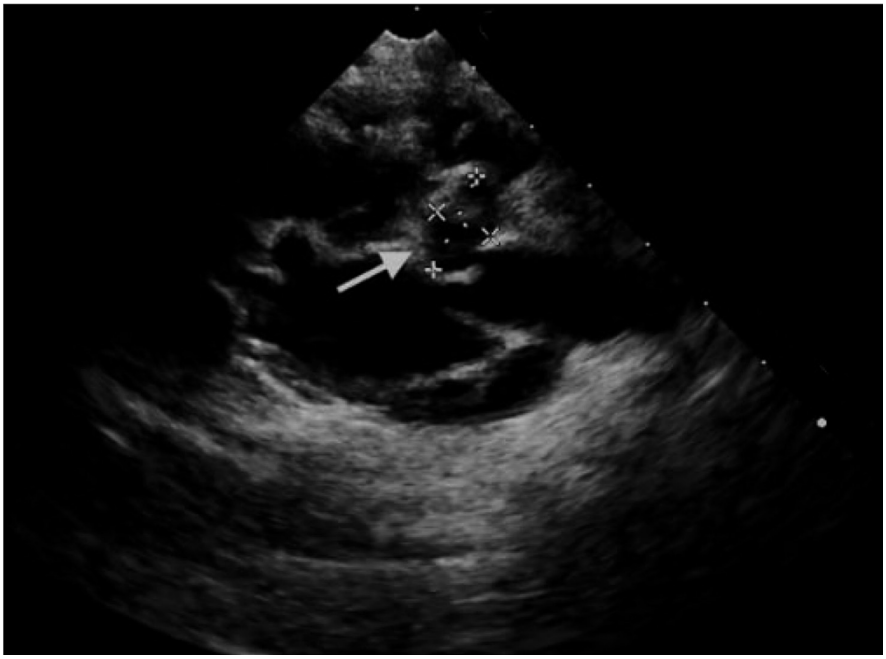

Fig. 1. Fusiform aneurysm with a size of 12x7 mm at the right coronary artery entrance.

After Henoch-Schönlein purpura, KD is the second most common vasculitis in childhood. Prolonged fever is usually the main symptom. Rashes, oral erythema, lymphadenopathy, conjunctivitis, oedema and desquamations are other common symptoms. Prompt IVIG treatment is required for preventing complications such as coronary aneurysms (6). Despite appropriate treatment, patients developed coronary aneurysms were reported (7). Moreover, macrophage activation syndrome was also reported among patients with IVIG resistant KD (8), and this contributes to the challenge of differentiation of KD and hyperinflammation related COVID-19.

Nowadays, COVID-19 is highly susceptive diagnosis among febrile patients and this may lead to misdiagnoses. Particularly KD can be easily confused with COVID-19 due to clinic and laboratory similarities (9). We think the main reason for the delay in the diagnosis of this patient is that the practitioners, in general, were more focused on COVID-19 than expected. Therefore, in this report, we respectfully aimed to remind caregivers that besides COVID-19, KD should be always kept in mind for children with persistent fever.

F. Haslak[1], *MD*
F. Karagozlu[2], *MD*
M. Yildiz[1], *MD*
A. Adrovic[1], *MD*
R. Dedeoglu[2], *MD*
O. Kasapcopur[1], *MD*

[1]Department of Paediatric Rheumatology, Istanbul University-Cerrahpasa, Cerrahpasa Medical School, Istanbul;
[2]Department of Paediatric Cardiology, Istanbul University-Cerrahpasa, Cerrahpasa Medical School, Istanbul, Turkey.

Please address correspondence to:
Ozgur Kasapcopur,
Department of Paediatric Rheumatology, Istanbul University-Cerrahpasa, Cerrahpasa Medical School, Istanbul, Turkey.
E-mail: ozgurkasapcopur@hotmail.com, ozgurkc@istanbul.edu.tr

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