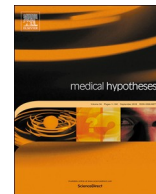




Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Letter to Editors

Kawasaki disease shock syndrome or toxic shock syndrome in children and the relationship with COVID-19



ARTICLE INFO

Keywords:

Kawasaki disease

COVID-19

SARS-CoV-2

Toxic shock syndrome

Pediatric

ABSTRACT

Most pediatric patients with COVID-19 are asymptomatic or show only mild symptoms. However, in the last two months, first in Europe and recently in the United States, a small number of children have developed a more severe inflammatory syndrome associated with COVID-19, which often leads to hospitalization and sometimes requires intensive care. A potential relationship was observed, especially between the occurrence of the Kawasaki disease and viral upper respiratory tract infections.

Most pediatric patients with COVID-19 are asymptomatic or show only mild symptoms. However, in the last two months, first in Europe and recently in the United States, a small number of children have developed a more severe inflammatory syndrome associated with COVID-19, which often leads to hospitalization and sometimes requires intensive care [1]. Pediatric patients affected by the new COVID-19 related syndrome show a condition of chronic fever, shock, toxic shock syndrome, and multi-organ failure. The tests carried out on COVID-19 in children with these syndromes do not always show the presence of infection [2]. There have been increasing reports of COVID-19-infected pediatric patients with symptoms and signs of Kawasaki syndrome in many sources [3,4]. Pediatric patients may have some or all of the characteristics of Kawasaki disease [5]. However, it should be remembered that in most cases, the diagnosis of Kawasaki disease is based on clinical criteria [6,7]. An important element confirming the diagnosis is demonstrating that the coronary arteries were involved in the disease process. Kawasaki disease etiological agent is still unknown, but its symptoms resemble many other virus childhood diseases, of which, for example, parvovirus B19 is suspected to be caused [8]. A potential relationship was observed, especially between the occurrence of the Kawasaki disease and viral upper respiratory tract infections.

The World Health Organization drew attention to an emerging and evolving problem at a press conference to report on reports of inflammatory shock in European countries and decided to take a closer look at the problem by collecting global data to understand the issue better and determine treatment; guidelines to help physicians deal with symptoms similar to Kawasaki's COVID-19 syndrome among pediatric patients were also being developed. Over ten days in mid-April 2020, the South Thames Retrieval Service in London recorded eight cases of hyperinflammatory shock with characteristics similar to atypical Kawasaki disease, Kawasaki disease shock syndrome, or toxic shock syndrome in pediatric patients. Four of the children were at risk of COVID-19 infection from their family, of which one was confirmed as having COVID-19 disease, and three were not infected. In addition, one infection was established in the remaining children, and one child tested positive for adenovirus and HERV. Shortly after these reports, Evelina London Children's Hospital's Intensive Care Unit already admitted over 20 children with similar clinical symptoms [9]. Also, the Pediatric Intensive Care Society (PICS) and the Health

Service Journal reported at the end of April 2020 that the number of children infected with COVID-19 has continued to increase, with multiple systemic inflammations and overlapping symptoms of toxic shock syndrome and unusual Kawasaki's disease in England. An alert issued on May 4, 2020, by the New York City Health Department stated the appearance of 15 cases of patients aged 2 to 15 years with typical symptoms of Kawasaki disease, Kawasaki shock syndrome, and atypical Kawasaki disease. Similar cases among pediatric patients have also been found in Italy at the hospital in Bergamo, where there are already more than 20 pediatric patients with a hyperinflammatory shock similar to that of Kawasaki syndrome (six times the expected annual result). Hyperinflammatory shock in children has also been observed in Spain and Portugal. The effects of coronaviruses on symptoms similar to Kawasaki syndrome and their association with this disease have already been studied with previously occurring types such as human coronavirus OC43/HKU1 and HCoV-NH. The study then demonstrated a link between Kawasaki's disease and coronaviruses, which may show us that COVID-19 can also be linked to it [10,11]; however, some other publications have not confirmed this relationship [11]. Due to the much higher number of infections and the ease of transmission, COVID-19 may pose a higher risk and hazard to pediatric patients for Kawasaki disease or Kawasaki-like symptoms. It should also be borne in mind that as a result of the COVID-19 pandemic, some Kawasaki disease cases, including those not related to SARS-CoV-2 in children, may be underdiagnosed or undergo delayed treatment [12]. Perhaps those cases might impact our understanding of Kawasaki syndrome origin and resolve the unknown reason for this clinical entity in the future.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.mehy.2020.109986>.

<https://doi.org/10.1016/j.mehy.2020.109986>

Received 19 May 2020; Accepted 7 June 2020

Available online 11 June 2020

0306-9877/ © 2020 Elsevier Ltd. All rights reserved.

References

- [1] Viner RM, Whittaker E. Kawasaki-like disease: emerging complication during the COVID-19 pandemic. *Lancet* 2020. [https://doi.org/10.1016/S0140-6736\(20\)31129-6](https://doi.org/10.1016/S0140-6736(20)31129-6).
- [2] Sardu C, Gambardella J, Morelli MB, Wang X, Marfella R, Santulli G. Hypertension, Thrombosis, Kidney Failure, and Diabetes: Is COVID-19 an Endothelial Disease? A Comprehensive Evaluation of Clinical and Basic Evidence. *J Clin Med* 2020. <https://doi.org/10.3390/jcm9051417>.
- [3] Jones VG, Mills M, Suarez D, et al. COVID-19 and Kawasaki Disease: Novel Virus and Novel Case. *Hosp Pediatr* 2020. <https://doi.org/10.1542/hpeds.2020-0123>.
- [4] Verdoni L, Mazza A, Gervasoni A, et al. An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study. *Lancet* 2020. [https://doi.org/10.1016/S0140-6736\(20\)31103-X](https://doi.org/10.1016/S0140-6736(20)31103-X).
- [5] Mahase E. Covid-19: concerns grow over inflammatory syndrome emerging in children. *BMJ* 2020. <https://doi.org/10.1136/bmj.m1710>.
- [6] Burns JC, Glode MP. Kawasaki syndrome. *Lancet* 2004;364:533–44.
- [7] Royle J, Burgner D, Curtis N. The diagnosis and management of Kawasaki disease. *J Paediatr Child Health* 2005;41:87–93.
- [8] Riphagen S, Gomez X, Gonzalez-Martinez C, Wilkinson N, Theocharis P. Hyperinflammatory shock in children during COVID-19 pandemic. *Lancet* 2020. [https://doi.org/10.1016/S0140-6736\(20\)31094-1](https://doi.org/10.1016/S0140-6736(20)31094-1).
- [9] Giray T, Biçer S, Küçük Ö, et al. Four cases with Kawasaki disease and viral infection: aetiology or association. *Infez Med* 2016;24:340–4.
- [10] Esper F, Shapiro ED, Weibel C, Ferguson D, Landry ML, Kahn JS. Association between a novel human coronavirus and Kawasaki disease. *J Infect Dis* 2005;191:499–502.
- [11] Chang LY, Chiang BL, Kao CL, et al. Kawasaki Disease Research Group. Lack of association between infection with a novel human coronavirus (HCoV), HCoV-NH, and Kawasaki disease in Taiwan. *J Infect Dis* 193, 283-286 (2006).
- [12] Harahsheh AS, Dahdah N, Newburger JW, et al. Missed or Delayed Diagnosis of Kawasaki Disease During the 2019 Novel Coronavirus Disease (COVID-19) Pandemic. *J Pediatr* 2020. <https://doi.org/10.1016/j.jpeds.2020.04.052>.

Michał Pruc

Faculty of Medicine, Lazarski University, Warsaw, Poland

Jacek Smereka

Department of Emergency Medical Service, Wrocław Medical University, Wrocław, Poland

Tomasz Dzieciatkowski

Chair and Department of Medical Microbiology, Medical University of Warsaw, Poland

Milosz Jaguszewski

First Department of Cardiology, Medical University of Gdansk, Gdansk, Poland

Krzysztof J. Filipiak

First Chair and Department of Cardiology, Medical University of Warsaw, Poland

Lukasz Szarpak*

Faculty of Medicine, Lazarski University, Warsaw, Poland

E-mail address: lukasz.szarpak@gmail.com.

* Address: Lazarski University, 43 Swieradowska Str. 02-662 Warsaw, Poland