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CASE BASED REVIEW

Kawasaki-like disease in children with COVID-19

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Abstract

Children with Coronavirus disease 2019 (COVID-19) are being reported to have manifestations of hyperinflammatory states and/or Kawasaki-like disease. In this study, we investigated children with typical and atypical Kawasaki disease (KD) likely to be associated with COVID-19. We have reported four children with Kawasaki-like disease probably associated with COVID-19. The clinical features were consistent with incomplete KD in three patients. SARS-CoV-2 RT-PCR was positive in one and the serology was positive in one patient with negative RT-PCR. Corticosteroids, anakinra, intravenous immunoglobulin (IVIG), and acetylsalicylic acid were used in the treatment. Three patients recovered after the treatment while one patient died. The literature review revealed 36 articles describing 320 children with Kawasaki-like disease associated with COVID-19. SARS-CoV-2 RT-PCR was negative in 120 (65.5%) of 183 patients while the serology was positive in 130 (83.8%) of 155 patients. The therapeutic options have included IVIG, acetylsalicylic acid, tocilizumab, anakinra, enoxaparin, and methylprednisolone. Pediatric COVID-19 cases may present with atypical/incomplete Kawasaki-like disease. Thus, pediatricians need to be aware of such atypical presentations resembling KD for early diagnosis of COVID-19.

Keywords COVID-19 · Kawasaki-like syndrome · 2019 novel coronavirus diseases · SARS-CoV-2 · Kawasaki disease

Introduction

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has affected individuals of all ages worldwide. Children constituted only a small proportion of patients with COVID-19, which was initially reported as 1.7% [1]. The actual incidence is unknown since there are no community-based studies. While more than 90% of children with COVID-19 were described to have asymptomatic, mild, or moderate disease, new concerns emerged with reports on hyperinflammatory states or Kawasaki-like disease [2, 3]. The resulting phenotypes are a combination of typical/atypical Kawasaki disease, Kawasaki shock syndrome, toxic shock syndrome, and macrophage activation syndrome/hemophagocytic lymphohistiocytosis [4, 5]. Children with hyperinflammatory syndrome and multiorgan involvement were classified as having pediatric inflammatory multisystem syndrome (PIMS) or multisystem inflammatory syndrome in children (MIS-C) [6, 7].

Kawasaki disease (KD) is an acute, systemic vasculitis of medium-sized vessels. Its etiology has not been clearly elucidated. Infectious triggers have been suggested in the etiology of KD due to having an epidemic pattern and marked seasonality [8]. Various infectious agents, including bacteria such as *Streptococcus pyogenes, Staphylococcus aureus*, and *Yersinia pseudotuberculosis*, and viruses such as adenovirus, enteroviruses, Epstein–Barr virus and

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coronavirus (New Haven coronavirus/HCoVNH) have been implicated in the etiology of KD [9–11]. Recently, along with the COVID-19 pandemic, Kawasaki-like disease associated with COVID-19 has been increasingly reported. Large case series of KD related to SARS-CoV-2 from the United Kingdom (UK), Italy, the United States of America (USA), and France were published [6, 12–17].

Kawasaki-like disease might be severe and requires more aggressive management. Herein, we report the characteristics of four patients with Kawasaki-like phenotype associated with COVID-19 from Turkey and analyze the features of similar published cases through a systematic literature review. We also discussed the effect of the local characteristics such as the presence of Bacillus Calmette–Guérin (BCG) vaccine in the routine vaccination schedule and high *MEFV* mutation carriage rate on disease course. Increasing reports of this phenotype from different countries would widen the spectrum of clinical and laboratory features, facilitate the diagnostic process, and provide more clues leading to early and effective treatment.

Search strategy

We performed a search through Pubmed/MEDLINE, Scopus and Web of Science databases using the following keywords: "Coronavirus disease-19", "COVID-19", "2019 novel coronavirus diseases", "severe acute respiratory syndrome coronavirus 2", "SARS-CoV-2", "2019-nCoV", "Kawasaki disease", "incomplete Kawasaki disease", "atypical Kawasaki disease", "Kawasaki-like disease", and "Kawasaki-like syndrome" filtered for articles published in English and Turkish. We searched the literature from inception to August 20, 2020. The systematic review was performed according to the PRISMA checklist (www.prisma-statement.org/). We included all articles that reported children who had Kawasaki-like disease associated with COVID-19. The schematic overview of the literature review process is shown in Fig. 1. The following parameters were noted from included studies: age, gender, country, diagnosis, and diagnostic tests for COVID-19. Diagnosis of complete KD was based on the criteria of the American Heart Association (AHA): the presence of fever for at least 5 days accompanied by the presence of at least four of the following five findings: bilateral non-exudative conjunctival injection, unilateral cervical lymphadenopathy, changes in the lips and oral cavity, skin rash, and changes in extremities, including indurative angioedema and desquamation [18]. Incomplete KD was diagnosed in the presence of unexplained prolonged fever, two or three diagnostic criteria, and supporting compatible laboratory or echocardiography (ECHO) findings [18].

Case presentations

Case 1 (admission: April 13, 2020)

A 7-year-old boy presented with fever, cough and an erythematous rash. He had bilateral conjunctival injection, diffuse erythematous maculopapular rash, erosive hyperemia of the oral mucosa, bilateral crackles on chest auscultation and respiratory distress findings in physical examination. Respiratory distress developed rapidly, and he was intubated due to hypoxemia. Laboratory tests revealed mild elevation of liver transaminases, lymphopenia, thrombocytopenia, elevated D-dimer, and lactate dehydrogenase levels. His ferritin level was within normal range when he was referred to our hospital on the 12th day of fever, but rose to 1336 µg/L (20–336) on day 27. The SARS-CoV-2 RNA was not detected from his nasopharyngeal swab. However, the bronchoalveolar lavage fluid tested positive for SARS-CoV-2 by real-time reverse transcriptase-polymerase chain reaction (RT-PCR). Chest computed tomography revealed bilateral diffuse ground-glass density areas.

Diffuse enlargement in the left coronary artery (diameter of the left coronary artery was 3.3 mm and *Z* score 2.0) with normal systolic function and pulmonary hypertension were reported in ECHO findings. The patient was diagnosed with incomplete KD and COVID-19 pneumonia. Intravenous immunoglobulin (IVIG), azithromycin, hydroxychloroquine, ritonavir and lopinavir, tocilizumab, and mesenchymal stem cell treatments were applied during his admission in the pediatric intensive care unit. On the 27th day of the onset of the fever, his hypoxia deteriorated under mechanical ventilation. He was started on venovenous extracorporeal membrane oxygenation (VV-ECMO) therapy. Disseminated intravascular coagulation, renal, and heart failure were developed in the follow-up. He died from severe hypoxia on the 17th day of VV-ECMO.

Case 2 (admission: July 11, 2020)

A 10-year-girl presented with resistant fever for the last 4 days, which was accompanied by vomiting. Physical examination was remarkable with one-sided submandibular lymphadenopathy size of 2 × 1.5 cm, changes in the lips and oral cavity, maculopapular erythema around the neck, bilateral non-exudative conjunctival injection, and diffuse abdominal tenderness. She had prolonged capillary refill time with hypotension. Inotropic therapy was initiated due to hypotensive values resistant to fluid therapy. Her laboratory examination revealed impairment of renal function,

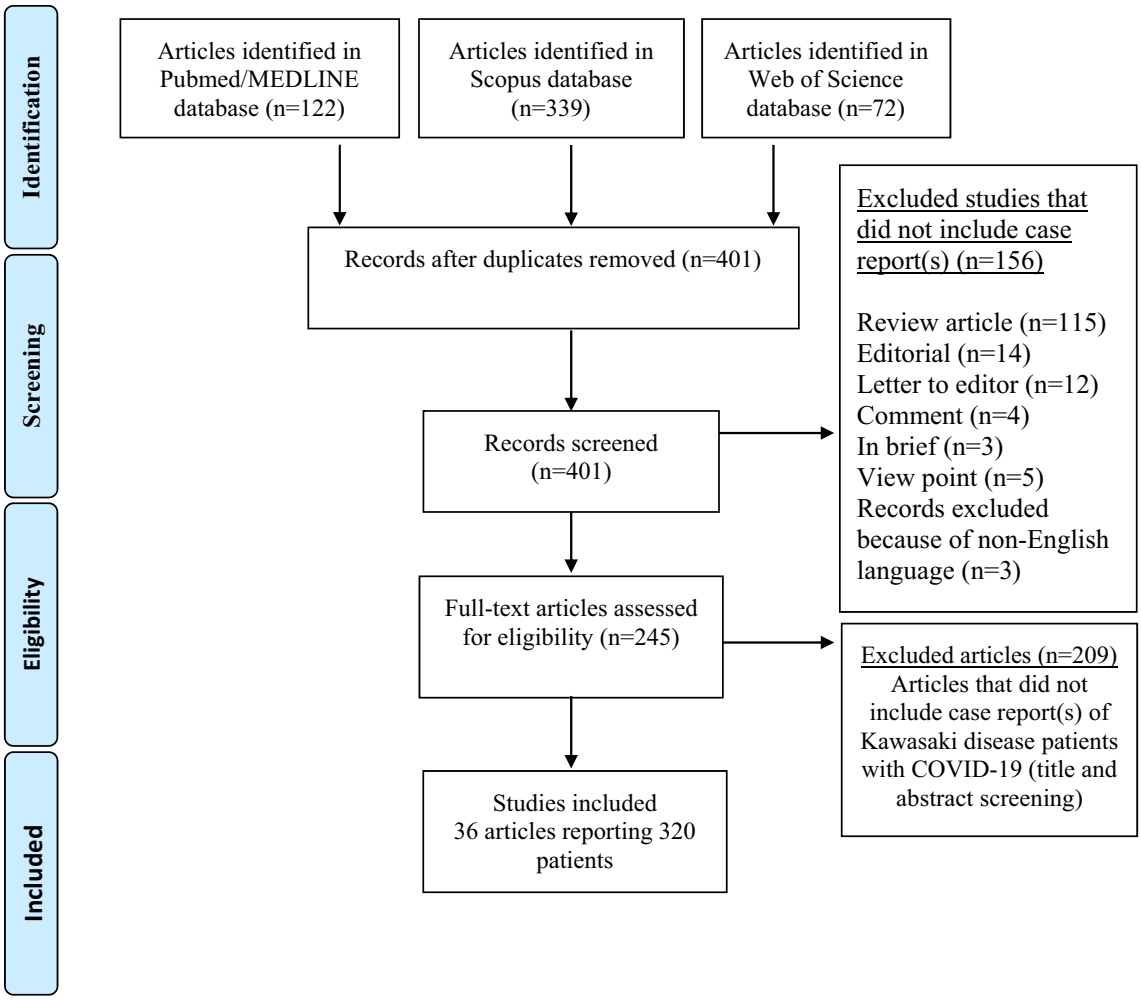

Fig. 1 Schematic overview of the studies reporting children with COVID-19-associated Kawasaki-like disease included in the literature research

high levels of acute phase reactants [C-reactive protein (CRP) 26.4 mg/dl (0–0.8), erythrocyte sedimentation rate (ESR) 96 mm/h (0–20)], lymphopenia with normal leukocyte count, normal platelet levels (155×10^3/μl), elevated brain-natriuretic peptide, D-dimer, ferritin (1019.6 μg/l) and triglyceride levels. Pleural effusion and ground-glass densities were evaluated in favor of COVID-19 in the thoracic tomography of the patient who developed respiratory distress in the follow-up. Besides, an edematous gall bladder was observed on abdominal tomography. She had no contact history for COVID-19, and the RT-PCR test result was negative. She was diagnosed with KD due to the fever and accompanying findings; the conjunctival injection, unilateral cervical lymphadenopathy, changes in the lips and oral cavity, and skin rash. ECHOc was normal. Intravenous immunoglobulin (IVIG), recombinant interleukin 1 (IL-1) receptor antagonist (anakinra), and corticosteroid therapies (20 mg/day) were administered due to the accompanying hyperinflammatory syndrome. The COVID-19 nasopharyngeal swab test result, which was examined for the second time, was negative, while serologic testing for IgG antibodies against SARS-CoV-2 was positive. Since the patient still had active symptoms, favipiravir treatment was started. On the 7th day of hospitalization, the inflammatory response and symptoms completely regressed, and the patient was discharged.

Case 3 (admission: May 22, 2020)

A 2-year-old girl presented with fever for 8 days. Edema of the dorsum of hands and feet accompanied fever. Arthritis was present in the proximal interphalangeal joints of the hands and right knee. She did not have a conjunctival injection, skin rash, or changes in the lips and oral cavity. Other system examination was unremarkable. The parents were actively working physicians.

Laboratory tests were as follows: leukocyte count 18×10^3/μl, neutrophil count 8.24×10^3/μl, platelet count

626×10^3/µl, CRP 10.196 mg/dl (< 0.1), ESR 69 mm/h (0–20), procalcitonin 0.093 ng/ml (0–0.1). COVID-19 nasopharyngeal swab test results were negative. Bone marrow examination was normal.

The echocardiographic evaluation revealed increased perivascular echogenicity in the right coronary artery. IVIG and acetylsalicylic acid treatment were initiated with the diagnosis of incomplete KD. Then low-dose corticosteroid treatment was started. She recovered within 2 weeks. SARS-CoV-2 serology testing could not be performed.

Case 4 (admission: May 16, 2020)

A 2-year-old girl with a diagnosis of congenital adrenal hyperplasia presented with resistant fever for 6 days. She had bilateral conjunctival injection at the onset of symptoms and conglomerate lymphadenopathy in the right cervical region. Clinical examination revealed no signs of hepatosplenomegaly or lymphadenopathy in other lymphatic regions. She had no skin rash, no changes in the oral cavity, or in the extremities. Her father was a physician.

Laboratory examination revealed elevated acute phase reactants [CRP: 13.66 mg/dl (0–0.5), ESR 57 mm/h (0–20)], and increased leukocyte count (17.4×10^3/µl). The initial ECHO examination was normal. COVID-19 nasopharyngeal swab test results were negative, two times. After consultations with the Departments of Pediatric Hematology-Oncology, Infectious Disease, and Cardiology, antibiotic treatment was initiated for lymphadenitis.

At 2-week follow-up, the ECHO findings revealed an aneurysm in the left coronary artery. The SARS-CoV-2 serology was negative, either. IVIG, acetylsalicylic acid, and corticosteroid treatment were initiated with the diagnosis of incomplete KD.

Discussion

An increasing number of Kawasaki-like disease in patients with COVID-19 continue to be reported worldwide. We have reported four patients, along with the review of 320 pediatric patients from the systematic literature search (Table 1) [6, 12–17, 19–47]. In addition to these articles presented in the table, six articles reported Kawasaki-like disease in children with COVID-19 [36, 48–52]. These articles were not included since there were no details about the reported patients. In our study, the clinical features were consistent with incomplete KD in three patients. SARS-CoV-2 RT-PCR was negative in all except one while the serology was positive in one patient with negative RT-PCR. Corticosteroids, anakinra, IVIG, and acetylsalicylic acid were used in the treatment. Three patients recovered after the treatment while one patient died. Until today, 80 patients were reported from France, 17 patients from Italy, 132 patients from the USA, 74 patients from the UK, 3 patients from India, 12 patients from Spain, 1 patient from Israel, and 1 patient from Turkey. SARS-CoV-2 RT-PCR was negative in 120 (65.5%) of 183 patients while the serology was positive in 130 (83.8%) of 155 patients. The therapeutic options included IVIG, acetylsalicylic acid, tocilizumab, anakinra, enoxaparin, and methylprednisolone. All of the reported patients recovered after the treatment except one.

Hacettepe University is a tertiary reference center for Pediatric Rheumatology, and we serve a large population of children, probably serving as the reference center for a large geographic area in Turkey. IgA-vasculitis/Henoch-Schönlein purpura is the most frequent childhood vasculitis in our region. In our hospital where we diagnosed 129 (complete and incomplete) KD patients between June 2007 and September 2019 (incidence 0.8 per month), 3 patients were diagnosed with KD within a month during the COVID-19 pandemic. Although an approximately 3.7-fold increase in the incidence of KD was observed in our hospital during the pandemic, it was lower compared to reported incidences from other countries [6, 12]. For instance, in the series reported from Italy, a 30-fold increased incidence of Kawasaki-like disease was reported, and it is expected to reach similar figures in North America [12].

3 of our 4 patients had clinical features consistent with incomplete KD. Along with the incomplete clinical features, they had very high CRP, lactate dehydrogenase, and D-dimer levels, which were different from our classical KD patients. The reported prevalence of incomplete KD is 15 to 36.2% [53, 54]. In the literature review, incomplete KD phenotype was increased to 45.9% ($n = 147$). Thus, the rate of incomplete KD during the pandemic is higher compared to the pre-COVID-19 period. The rate could differ in different geographic areas. In our center in the pre-COVID period, Aydin et al. had reported the prevalence of incomplete KD of our center as 48.0% [55]. The rate increased to 75.0% ($n = 3$) in patients during the COVID-19 pandemic [55]. This finding suggests that we should maintain a high index of suspicion for incomplete KD in COVID-19 patients.

The underlying mechanisms of cardiovascular involvement in COVID-19 are currently unknown. However, Varga et al. reported that infected endothelial cells stimulate the inflammatory response and cause endotheliitis as a result of viral exposure [56]. Besides the viral effects, host factors are important in the pathogenesis of KD. Certain genetic or environmental factors may be suggested for the rather lower frequency of these cases in our center. First, the carrier frequency of *MEFV* mutations is high in our country, with a rate of 1/5 [57]. Asymptomatic heterozygous carriers of *MEFV* mutations have been indicated to have more frequent inflammatory symptoms, increased CRP, serum amyloid-A protein and the mRNAs for proinflammatory cytokines such

Table 1 Clinical features of patients with Kawasaki-like disease associated with COVID-19

First author [reference number]	Country	Number of patients	Age (years)	Gender	Diagnosis	Diagnostic tests results for COVID-19	Death (yes/no)
Jones [19]	USA	1	6 months	F	Complete KD	Positive RT-PCR test (nasopharyngeal swab)	No
Licciardi [20]	Italy	2	7, 12	M	Complete KD Kawasaki-like Hyperinflammatory Syndrome	Negative nasal swabs for COVID-19 Positive serologic antibody testing in all patients	No
Verdoni [12]	Italy	10	7.5 [SD 3·5]	7M 3F	(5 incomplete, 5 complete KD) KDSS in 5 patients	Positive nasal swab for COVID-19 in 2 patients Positive serologic tests in 8 of 10 patients (IgG or IgM, or both)	No
Rivera-Figueroa [21]	USA	1	5	M	Incomplete KD KDSS	Positive RT-PCR result from nasopharyngeal swab	No
Leon [22]	USA	1	6	F	Incomplete KD Kawasaki- like Hyperinflammatory Syndrome	Positive nasopharyngeal swab for COVID-19	No
Labé e [23]	France	1	3	M	Complete KD	Negative COVID-19 RT-PCR test	No
Chiotos et al. [24]	USA	6	7.5 (5–14)	5F 1M	Incomplete KD in all patients MIS-C in all patients	Positive nasopharyngeal SARS-CoV-2 RT-PCR in 3 patients Positive serologic antibody testing in 5 patients	No
Waltuch [25]	USA	4	11 (5–13)	3M 1F	Incomplete KD TSS	Negative by nasopharyngeal RT-PCR swab in all patients Positive serologic antibody testing in all patients	No
Yozgat [26]	Turkey	1	3	F	Complete KD PMIS	Negative COVID-19 RT-PCR test	No
Rauf [27]	India	1	5	M	Incomplete KD TSS	Negative COVID-19 RT-PCR test	No
Toubiana [6]	France	21	7.9 (3.7–16.6)	12F 9M	11 complete KD 10 incomplete KD KDSS in 12 patients	Positive nasopharyngeal SARS-CoV-2 RT-PCR in 8 patients Positive SARS-CoV-2 serum serology in 19 patients	No
Riphagen [13]	UK	8	8.8 (6–14)	3F 5M	Incomplete KD Hyperinflammatory shock	Negative COVID-19 RT-PCR test (BAL and nasopharyngeal samples) Positive SARS-CoV-2 serum serology in all patients	Yes (1 patient)
Grimaud [14]	France	20	10 (2.9–15)	10F 10M	Atypical KD Hyperinflammatory shock	Positive SARS-CoV-2 RT-PCR in 10 patients Positive SARS-CoV-2 serology in 15 children	No

Table 1 (continued)

First author [reference number]	Country	Number of patients	Age (years)	Gender	Diagnosis	Diagnostic tests results for COVID-19	Death (yes/no)
Pouletty [15]	France	16	10 IQR (4.7–12.5)	8F 8M	10 complete KD 6 incomplete KD KDSS in 7 patients	Positive SARS-CoV-2 RT-PCR in 11 patients Positive serologic tests in 7 of 8 patients (IgG)	No
Dasgupta [28]	USA	1	8	F	Complete KD KDSS	Negative COVID-19 RT-PCR test Negative SARS-CoV-2 serology	No
Feldstein [16]	USA	74	5.7 (1.7–8.9) for complete KD 8.4 (4.2–12.0) for incomplete KD	NA	38 complete KD 36 incomplete KD	NA	NA
Whittaker [29]	UK	13	8 (5–11)	10M 3F	13 complete KD	Negative COVID-19 RT-PCR test Positive serologic tests in 8 of 12 patients (IgG)	No
Greene [30]	USA	1	11	F	Incomplete KD	Positive SARS-CoV-2 RT-PCR	No
Ferrero [31]	Italy	4	3, 7, 9, 16	3M 1F	Incomplete KD	Positive nasopharyngeal SARS-CoV-2 RT-PCR in 2 patients	No
Ng [32]	UK	3	13, 16, 17	2M 1F	Incomplete KD	Positive SARS-CoV-2 RT-PCR in 1 of 3 patients Positive serologic tests in 2 patients	No
Davies [17]	UK	28	11 (7–13)	16M 12F	NA	NA	NA
Ramcharan [33]	UK	15	8.8 (6.4–11.2)	11M 4F	7 complete KD 8 incomplete KD	Positive SARS-CoV-2 RT-PCR in 2 patients Positive serologic antibody testing in all patients	No
Cheung [34]	USA	13	NA	NA	8 complete KD 5 incomplete KD	NA	No
DeBiasi [35]	USA	1	4	M	Incomplete KD KDSS	Positive COVID-19 RT-PCR test (lower respiratory specimen)	No
Capone [36]	USA	21	NA	NA	Complete KD	NA	No
Ouldali [37]	France	10	10.2 (1.5–15.8)	4M 6F	5 complete KD 5 incomplete KD	Positive SARS-CoV-2 RT-PCR in 5 of 9 patients Positive serologic tests in 5 of 6 patients	No
Blondiaux [38]	France	4	9 (6–12)	1M 3F	Incomplete KD	Negative SARS-CoV-2 RT-PCR in all patients Positive serologic tests in all patients	No
Perez-Toledo [39]	UK	7	NA	NA	NA	Negative SARS-CoV-2 RT-PCR in all patients Positive serologic tests in all patients	No
Raut [40]	India	1	5-month	M	Incomplete KD	Positive SARS-CoV-2 RT-PCR	No

Table 1 (continued)

First author [reference number]	Country	Number of patients	Age (years)	Gender	Diagnosis	Diagnostic tests results for COVID-19	Death (yes/no)
Chiu [41]	USA	1	10	M	Incomplete KD	Positive SARS-CoV-2 RT-PCR	No
Lee [42]	USA	7	8 (1–17)	NA	2 complete KD 5 incomplete KD	Positive SARS-CoV-2 RT-PCR in 4 patients Positive serologic tests in all patients	No
Cazzaniga [43]	Italy	1	6	M	Incomplete KD	Positive SARS-CoV-2 RT-PCR	No
Regev [44]	Israel	1	16	M	Incomplete KD	Positive SARS-CoV-2 RT-PCR Positive serologic tests	No
Gupta [45]	India	1	7	F	Complete KD	Negative SARS-CoV-2 RT-PCR	No
Pino [46]	Spain	12	NA	6M 6F	7 complete KD 5 incomplete KD	Positive SARS-CoV-2 RT-PCR in 4 of 12 patients Positive serologic tests in 6 of all patients	No
Ouldali [47]	France	8	11.5	5F 3M	4 complete KD 4 incomplete KD	Positive SARS-CoV-2 RT-PCR in 5 of 8 patients Positive serologic tests in 7 of 8 patients	No
Presented patients in this report	Turkey	4	2,10, 2,7	3F 1M	1 complete KD 3 incomplete KD PMIS in two patients	Negative nasopharyngeal COVID-19 RT-PCR test in all patients BAL fluid tested positive for SARS-CoV-2 by RT-PCR in a patient Positive SARS-CoV-2 serology in a patient and negative in another	Yes (1 patient)

BAL bronchoalveolar lavage, *F* female, *KD* Kawasaki disease, *KDSS* Kawasaki disease shock syndrome, *M* male, *MIS-C* multisystem inflammatory syndrome in children, *PMIS* pediatrics multisystem inflammatory syndrome, *RT-PCR* real-time reverse transcriptase-polymerase chain reaction, *TSS* toxic shock syndrome

as tumor necrosis factor, IL-1, IL-6 and IL-18 [58–60]. In one previous report, the authors also commented on a protective effect of *MEFV* variants against COVID-19 [58]. Such *MEFV* mutation carriers with subclinical inflammation may be protected against endemic infections due to the increased activity of the pyrin [60, 61]. A selective advantage against some pathogens such as *Yersinia pestis* in *MEFV* mutation carriers has recently been proposed [62]. The jury is out on whether FMF carriage might provide some protection against COVID-19 infection. Another issue is the possible protective effect of BCG vaccine [63]. BCG vaccine is included in the routine vaccination program in Turkey, and it is applied at two months of age. Previous studies have shown that the BCG vaccine protects against other viral infections by causing metabolic and epigenetic changes that increase the innate and trained immune response to infections [64]. Supporting this information, Arts et al. reported that BCG vaccination reduced yellow fever vaccine viremia by 71% [65]. On the other hand, the duration of the BCG effect remains uncertain. Long-term studies are needed with a broader analysis of monocyte function [65, 66]. However, the apparent lack of protection against COVID-19 was observed in the UK and France, where BCG vaccination was administered to older children [67]. It is hypothesized that when vaccination is done in the early infancy period, it may result in improved immune surveillance for lifelong, resulting in a milder viral disease. But if performed at an older age, this response may be short term or insufficient [67]. Finally, early measures such as curfews in children and travel restrictions might have an effect in reducing the spread of viruses and decreased incidence of KD.

We have not been able to show COVID-19 in two of our patients. Both parents of these two patients were actively practicing physicians at the time of the pandemics. RT-PCR-based assays performed on respiratory specimens were positive in 63 of 183 patients (34.5%) with KD and COVID-19. The sensitivity of RT-PCR tests is low, and it is affected by many external factors such as the sampling time, whether the sample is taken correctly, and the performance of the kits [68]. Ai et al. reported that 413 of 1014 (41%) RT-PCR test results of infected patients were negative at the initial presentation [69]. Although Waltuch et al. reported negative RT-PCR results of nasopharyngeal swab samples in four patients, serological tests of these patients were positive [25]. Serological tests have some advantages compared to RT-PCR tests such as presence of antibodies in the blood for a long time, unlike viral RNA, and stable structure of antibodies in sample processing steps. However, serological tests could be negative in the infected patients at an early stage of infection [70]. In our literature review, serologic tests were performed in 155 patients and 130 were positive (83.8%). The sensitivity of COVID-19 serology tests ranges from 72.7 to 100% [71].

Some children with COVID-19 developed a cytokine storm syndrome which may require intensive care [72]. Children with persistent fever, inflammation (neutrophilia, high CRP, and lymphopenia), and single or multi-organ dysfunction have been identified in the UK as "Pediatric Multisystem Inflammatory Syndrome in relation to SARSCoV-2 (PMIS-TS)" regardless of the SARS-CoV-2 RT-PCR test results [73]. This hyperinflammatory condition was named as "Multisystem Inflammatory Syndrome in Children (MIS-C)'' by the Centers for Disease Control and Prevention [74]. The phenotypes under this category are typical/atypical KD, Kawasaki shock syndrome, toxic shock syndrome, and macrophage activation syndrome/hemophagocytic lymphohistiocytosis [4]. In this study, we investigated only the group with typical/atypical KD accompanying COVID-19, to compare with our previous figures for KD: our first patient with incomplete KD also developed a hyperinflammatory syndrome.

During the COVID-19 pandemic, healthcare workers are worried about passing the infection to their families. The parents of two of our patients were healthcare workers who were at high risk to contact with infected patients. Similarly, healthcare workers were present in families of one every two patients in the study by Licciardi et al. [20]. Similarly, in early reports from China, 40 of 138 (29%) patients were healthcare professionals [75].

Conclusion

We present our patients with KD-like disease associated with SARS-CoV-2 infection. Since pediatric cases may come with findings consistent with atypical or incomplete KD, pediatricians need to be aware of such atypical presentations of COVID-19 infection for early diagnosis. A high clinical suspicion should be maintained for COVID-19-associated Kawasaki-like disease since it usually requires aggressive management. We await further studies to explain the clinical course of pediatric patients diagnosed with COVID-19 and KD, in particular, to clarify the pathophysiology. Whether there are geographic or ethnic factors affecting the occurrence of a Kawasaki-like disease in these patients will also be explained with further reports.

Author contributions Dr. UKA conceptualized and designed the study, drafted the initial manuscript, reviewed and revised the manuscript. Dr. SK conceptualized and designed the study, coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content. Dr. YO conceptualized and designed the study, drafted the initial manuscript, reviewed, and revised the manuscript. Dr. HHA conceptualized and designed the study, drafted the initial manuscript, reviewed, and revised the manuscript. Dr. EDB conceptualized and designed the study, coordinated and supervised data collection, critically reviewed, and revised the manuscript. Dr. EA conceptualized and designed the study, drafted the initial manuscript, reviewed, and revised the manuscript. Dr. SD conceptualized and designed the study, drafted the initial manuscript, reviewed, and revised the manuscript. Dr. ES conceptualized and designed the study, coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content. Dr. DV conceptualized and designed the study, coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content. Dr. BB conceptualized and designed the study, coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content. Dr. YB conceptualized and designed the study, coordinated and supervised data collection, and critically reviewed and revised the manuscript. Dr. SO conceptualized and designed the study, coordinated and supervised data collection, and critically reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Compliance with ethical standards

Conflict of interest The authors have indicated that they do not have any financial and non-financial potential conflicts of interest to disclose.

Informed consent Written informed consent was obtained from the presented patients and their parents.

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