COVID-19 and Kawasaki Disease: Novel Virus and Novel Case

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Abstract

In the midst of the coronavirus disease (COVID-19) pandemic, we are seeing widespread disease burden affecting patients of all ages across the globe. However, much remains to be understood as clinicians, epidemiologists, and researchers alike are working to describe and characterize the disease process while caring for patients at the frontlines. We describe the case of a 6-month-old infant admitted and diagnosed with classic Kawasaki disease (KD), who also screened positive for COVID-19 in the setting of fever and minimal respiratory symptoms. The patient was treated per treatment guidelines, with intravenous immunoglobulin (IVIG) and high-dose aspirin (ASA), and subsequently defervesced with resolution of her clinical symptoms. The patient's initial echocardiogram was normal, and she was discharged within 48 hours of completion of her IVIG infusion, with instruction to quarantine at home for 14 days from the date of her positive testing for COVID-19. Further study of the clinical presentation of pediatric COVID-19 and the potential association with KD are warranted, as are the indications for COVID-19 testing in the febrile infant.

INTRODUCTION

The rapid spread of Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has led to a global pandemic, with infected individuals of all ages residing in almost every country in the world. The pediatric population appears to be affected in much smaller proportions than adults, with only 2% of cases described in patients under age 20.[1] An epidemiologic report described 731 confirmed COVID-19 cases in the pediatric population, with over 90% of patients characterized as asymptomatic, mild, or moderate cases.[2] This study looked at a total of 2143 patients, 1412 of whom had suspected but unconfirmed COVID-19 infection, but there was little description of co-incidence of other clinical conditions, and no cases reported of concurrent Kawasaki disease (KD).

We describe here the case of a pediatric patient diagnosed and treated for classic KD in the setting of confirmed COVID-19 infection, published with parental permission.

CASE DESCRIPTION

The patient is a 6-month-old, full term, previously healthy and fully immunized female who initially presented to pediatric urgent care with one day of fever, fussiness, and refusal to eat. She did not exhibit cough, congestion or rhinorrhea. Examination showed a fussy infant with a temperature of 38.8°C, with no focal signs of infection. Laboratory evaluation included a rapid influenza swab and a catheterized urinalysis with urine culture, all of which were negative. She was diagnosed with a viral infection.

On day 2 of fever, she developed an erythematous, seemingly non-pruritic, blotchy rash.

She re-presented to urgent care on day 4 of fever with persistent rash. Although she remained free of cough, there was possible mild congestion. Vital signs showed temperature of 38.3°C, sinus tachycardia (200 beats/minute), and tachypnea with an oxygen saturation of 100%. Examination was notable for

irritability, limbic-sparing conjunctivitis, and dry cracked lips. There was no appreciable lymphadenopathy and at the time she had normal extremities. She had mild subcostal retractions, though normal breath sounds. Laboratory testing showed a left-shifted white blood cell count with bandemia, normocytic anemia, normal platelets, markedly elevated c-reactive protein 13.3 mg/dL, and erythrocyte sedimentation rate 118 mm/hr. She had hyponatremia (sodium 133 mEq/L) and hypoalbuminemia (albumin 2.8 g/dL), with otherwise normal chemistries including liver function tests. Respiratory pathogen testing by reverse transcription polymerase chain reaction test (RT-PCR) and blood culture were negative. A chest x-ray showed a faint opacity in the left midlung zone. Throughout this period of illness, she had no sick contacts. Her 9-year-old sibling had upper respiratory symptoms 3 weeks prior. The family had self-isolated due to the COVID-19 pandemic for the week prior, without leaving home for school or work. There was no history of recent travel.

The patient was referred for admission for KD evaluation. Given her fever, possible mild congestion, and chest x-ray findings, she was sent to the emergency department for COVID-19 testing prior to admission to the pediatric floor. Upon arrival, the patient was on day 5 of fever, had limbic sparing conjunctivitis (Figure 1), prominent tongue papilla, a blanching, polymorphous, maculopapular rash (Figure 2), and swelling of the hands (Figure 3) and lower extremities—thus meeting classic criteria for KD. She was treated with a single dose of 2g/kg intravenous immunoglobulin (IVIG) and high dose acetylsalicylic acid (ASA 20mg/kg four times daily) according to treatment guidelines.[3] Her last elevated temperature was 38.3°C just after completing IVIG. An echocardiogram was normal without any evidence of coronary dilation or aneurysm, no pericardial effusion, and with normal valvar and ventricular function.

The evening prior to discharge, RT-PCR testing for COVID-19 resulted positive from the Stanford Clinical Virology Laboratory. The Public Health Department was notified, and the family was instructed to quarantine at home for 14 days from positive test date. She was discharged on low dose ASA

(3mg/kg daily) with plans to follow-up with pediatric cardiology for repeat echocardiographic evaluation two weeks after discharge, timed to occur after the mandated 14-day quarantine.

DISCUSSION

To our knowledge, this is the first described case of KD with concurrent COVID-19 infection. KD is an acute vasculitis of childhood and the leading cause of acquired heart disease in children in developed countries, with 50% of cases occurring in those <2 years of age, and 80% in those <5 years of age.[4] The diagnosis of "classic" KD is considered in patients presenting with fever for 5 days together with at least 4 out of 5 clinical criteria in the absence of an alternate diagnosis.

The cause of KD remains unknown, despite several decades of investigation. Some evidence suggests an infectious trigger, with winter-spring seasonality of the disease, and wave-like spread of Japanese epidemics of KD.[4] Various studies have described an association between viral respiratory infections and KD, ranging from 9% to as high as 42% of patients with KD testing positive for a respiratory viral infection in the 30-days leading up to diagnosis of KD.[5-7] Interestingly, Turnier *et al.* in 2015 described that 28% of positive results were attributable to rhinovirus/enterovirus, 8.7% due to parainfluenza, and the remaining pathogens: respiratory syncytial virus, influenza, adenovirus and human coronavirus (strains 229E, HKU1, NL63, OC43) were each positive less than 5% of the time.[5]

Although the clinical significance of our patient's positive COVID-19 testing in the setting of her KD is not clear, her testing for COVID-19 appears accurate. The Stanford Health Care Clinical Virology Laboratory serves pediatric and adult tertiary care hospitals and affiliated clinics in Northern California. In early January 2020, two multiplex RT-PCR assays were validated based on a modified published protocol.[8] These assays target the envelope and RNA-dependent RNA-polymerase genes, respectively. Analytical sensitivity from nasopharyngeal swabs eluted in viral transport medium was shown to be good with a lower limit of detection ranging between 500-700 copies/mL. Furthermore, analytical specificity was high with

no cross-reactivity observed in over 50 tested samples with seasonal coronaviruses or other respiratory viruses. Samples showing late cycle threshold (CT) values (CT≥40) are repeated for confirmatory testing to prevent false-positive results. Although direct comparison data between this assay and the CDC assay—which targets two regions of the nucleocapsid gene—have not yet been published, preliminary data suggest similar analytic performance.[8,9]

At the time of this patient's hospital discharge, the World Health Organization reported almost 180,000 global cases of confirmed COVID-19 with 7,426 deaths.[10] Despite the growing number of reported cases there remains a knowledge gap regarding the infectious, epidemiologic and clinical features associated with COVID-19 illness, particularly in the pediatric population. To date, the most common pediatric presentation of COVID-19 is an array of signs and symptoms including completely asymptomatic to symptoms of acute upper respiratory tract infection such as fever, fatigue, cough, sore throat, rhinorrhea and congestion, and shortness of breath. In more severe cases, symptoms can include gastrointestinal symptoms and patients can progress to respiratory failure, shock, coagulation dysfunction, and renal injury.[2]

With regards to her COVID-19 infection, our patient's clinical course and presentation were mild. Throughout her hospitalization, she did not have any notable respiratory symptoms and repeat chest x-ray was not obtained. Her mother was in close contact with the infant throughout hospitalization and has no respiratory symptoms as of 2 weeks post hospital discharge. When coronary involvement appears with KD, it typically occurs after the initial presentation. As such, recommendations for monitoring include echocardiography in 1-2 weeks and 4-6 weeks after treatment.[3]

As we continue to see the spread of COVID-19 and increase in cases worldwide, clinical criteria for testing for COVID-19 may be restricted to those with respiratory symptoms due to constraints such as testing availability. In pediatrics, with the clinical spectrum yet to be clearly defined, patients presenting with fever alone or primarily with other organ system involvement such as gastrointestinal symptoms may be missed if testing is restricted to those with respiratory complaints alone.

CONCLUSION

This case report may serve as a useful reference to other clinicians caring for pediatric patients affected by COVID-19 as understanding of the clinical presentation patterns continue to evolve. Further description of the clinical course of pediatric patients diagnosed with COVID-19 remains necessary, particularly regarding the potential association with KD.

Acknowledgments

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FIGURES

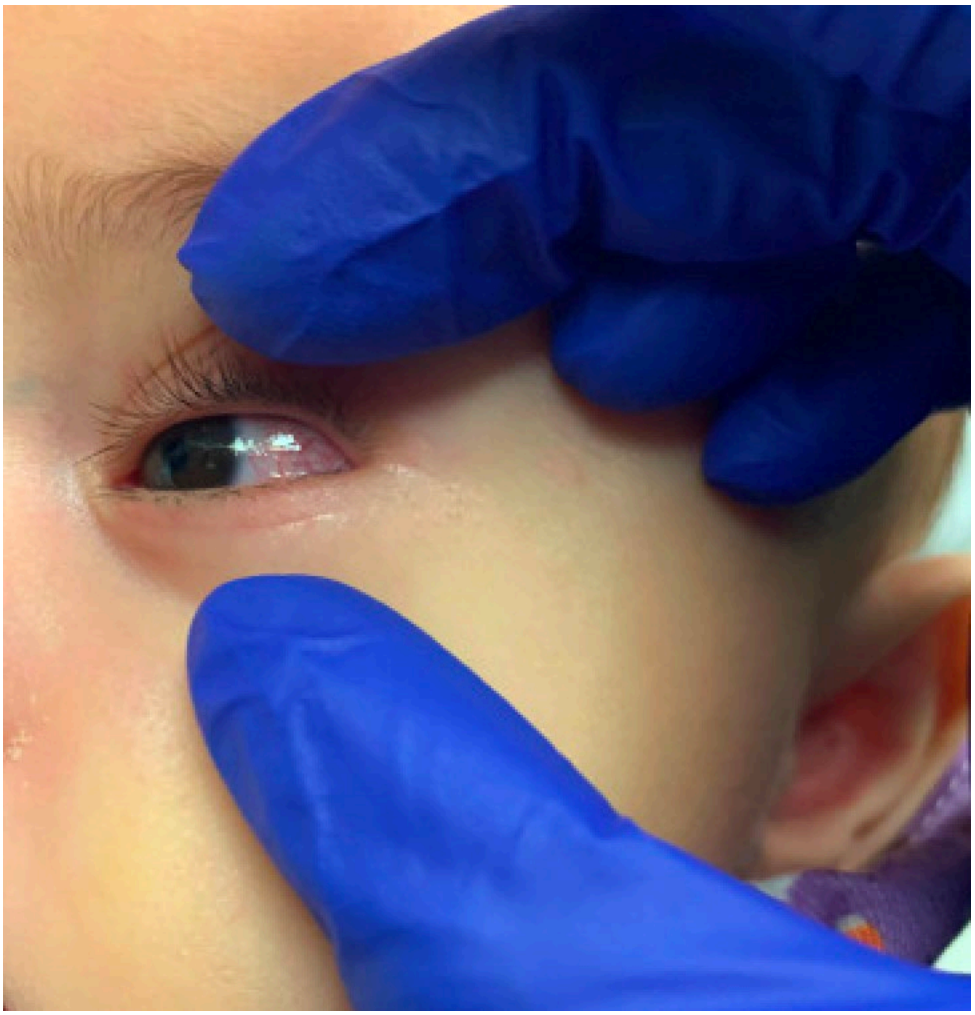

Figure 1. Bulbar conjunctival injection. Image shared with parental permission.

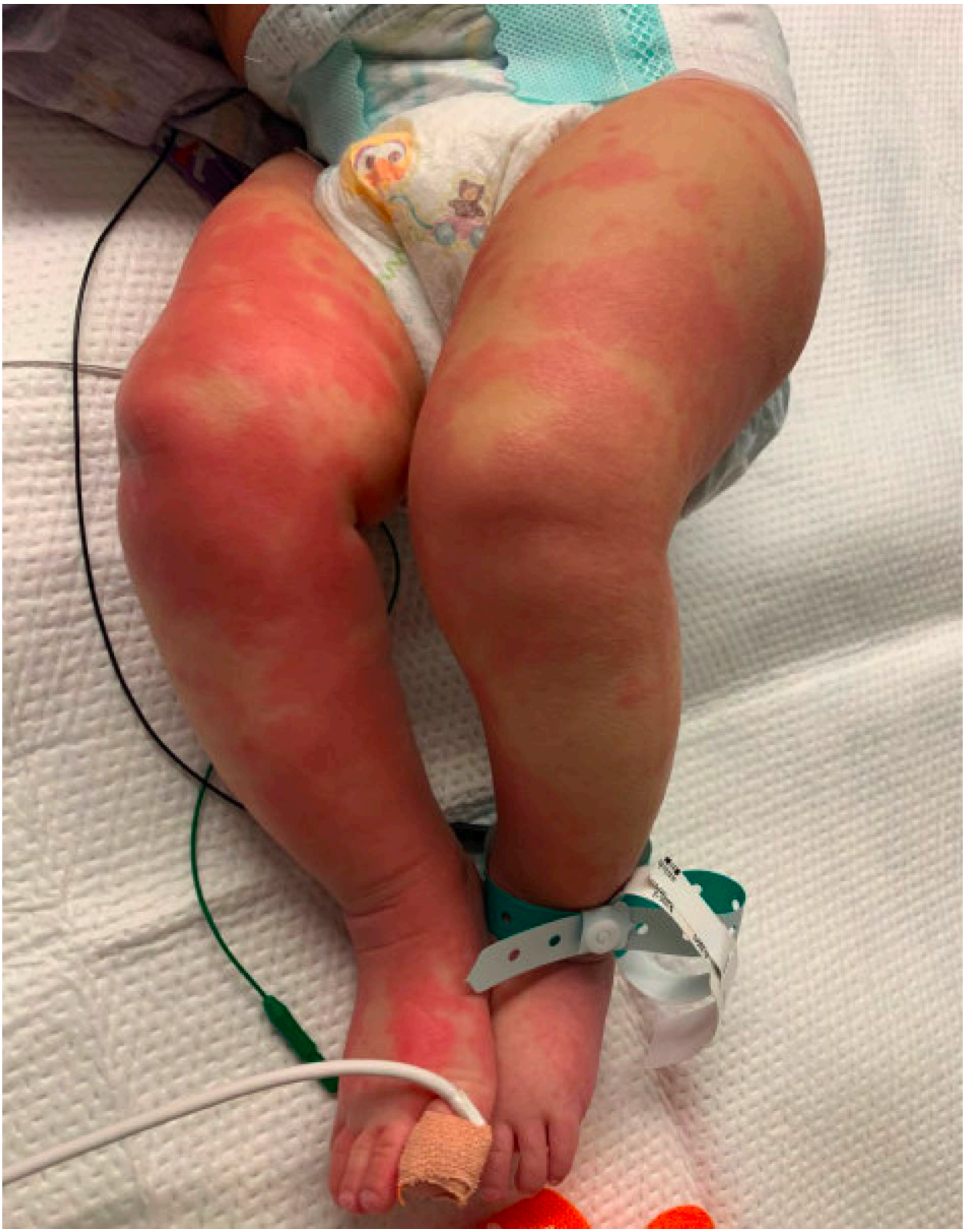

Figure 2. Maculopapular rash. Image shared with parental permission.

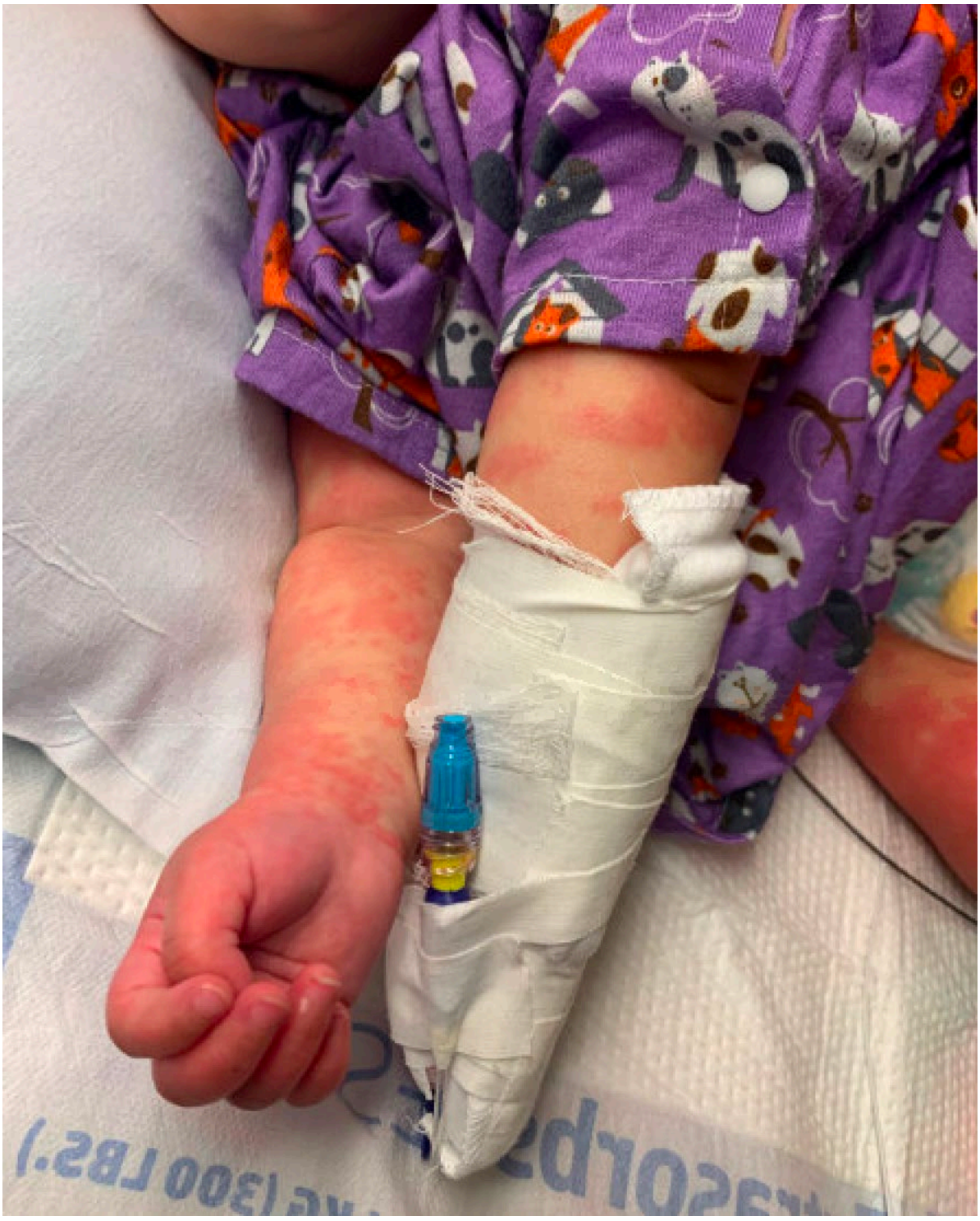

Figure 3. Upper extremity erythema and edema. Image shared with parental permission.

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