

Fever without a source in a young infant due to SARS-CoV-2

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Contributors' Statement Page Drs. Kan, Grant, Muña, and Greenhow: acquired, analyzed, and interpreted the data; drafted the initial manuscript; and reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

ABSTRACT

A 5-week-old infant admitted for fever without a source subsequently tested positive for SARS-CoV-2. She had a mild hospital course without respiratory distress. This unexpected presentation changed regional hospital screening for COVID-19 and personal protective equipment use by medical providers evaluating infants with fever without a source.

Keywords: fever, infant, COVID-19, SARS-CoV-2

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Abbreviations:

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

COVID-19: coronavirus disease

PPE: Personal protective equipment

KPNC: Kaiser Permanente Northern California

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Case Presentation

Since its identification in January 2020, the impact of the COVID-19 pandemic has been profound with over 590,000 cases worldwide and over 100,000 confirmed cases in the United States, which has now surpassed all other countries worldwide [1]. Thus far, there have been relatively few pediatric cases worldwide with critical disease requiring hospitalization [2] and the focus has been on adults with severe respiratory symptoms. Infection in children has been therefore poorly characterized, and very little is known about the clinical course in young infants. Here we present a case of a young infant admitted for fever without a source that was subsequently found to have SARS-CoV-19. Our experience with this case has important implications for the evaluation for infant fever without a source and public health implications for community and healthcare associated infections.

An ex-full term 5-week-old female with a history of hydronephrosis and duplex kidney, but otherwise developing well infant presented to the Kaiser Permanente Northern California (KPNC) San Francisco Emergency Department (ED) in March 2020 with symptoms of fever to 100.4°F and somnolence without respiratory distress. She had been breastfeeding well, voiding normally, and otherwise acting well. The patient had known sick contacts, including her father, who co-presented to the ED for five days of fever, myalgias, mild cough, coryza, and pharyngitis without shortness of breath. He reported inability to taste and smell. He had previously presented to urgent care four days prior with these symptoms and had been treated empirically with oseltamivir. The father did not have known sick

contacts but works in a client-facing capacity in the restaurant industry. Due to the hospitalization of the patient, her father was tested for SARS-CoV-2. The patient's mother reported that she had subsequently developed very similar symptoms including fever, myalgia, upper respiratory symptoms, anosmia, and ageusia.

On initial physical examination, the infant was febrile with a temperature of 38°C and tachycardic with a pulse of 179. The patient was otherwise well appearing and no focal signs of infection were observed. Notably, she had a normal respiratory rate and effort with clear lungs. A complete blood count revealed leukopenia (3,000 cells/ μ L), lymphopenia (1,050 cells/ μ L), neutropenia (1,000 cells/ μ L), normocytic anemia (hemoglobin 10.6 g/dL, hematocrit 31.4%, mean corpuscular volume 94 fL), and normal platelets (204×10^3 cells/ μ L). Due to the infant's age and presentation of fever without a source in the setting of leukopenia, a full infant sepsis evaluation was initiated [3]. A urinalysis demonstrated trace hemoglobin and protein but was otherwise normal. The C-reactive protein was not elevated. A lumbar puncture was performed with cerebrospinal fluid (CSF) studies that were unremarkable. Urine, blood, and CSF cultures ultimately demonstrated no growth for bacterial organisms. Out of concern for the parents' respiratory symptoms, influenza and respiratory syncytial virus RT-PCR were sent and resulted negative. Due to a lack of respiratory symptoms, the patient was not initially tested for SARS-CoV-2.

At presentation, the infant received a 20ml/kg normal saline bolus and supportive care. Within hours of hospitalization, her father's test results returned positive for SARS-CoV-2; subsequently a combination oropharyngeal and bilateral nasopharyngeal swab (three sites to increase sensitivity) from the patient were sent for qualitative nucleic amplification for SARS-CoV-2 (Roche cobas 6800/8800) and resulted positive the same day. At the time SARS-CoV-2 testing was sent, the patient was placed on contact and droplet precautions with eye protection. She was treated empirically with intravenous ceftriaxone given her leukopenia

and elevated risk for urinary tract infection, but this was stopped after the urine and blood cultures, which were obtained prior to antibiotics, showed no growth at 24 hours. Acetaminophen was administered as an antipyretic and for discomfort as needed. The baby continued to breastfeed while the mother wore a mask. The infant had a very mild clinical course with resolution of fever within about 30 hours of hospitalization. The infant was observed to have an intermittent dry cough while crying, but otherwise had no increased work of breathing or respiratory distress and did not require supplemental oxygen. She was discharged on hospital day three with a plan for the family to isolate until seven days from onset of symptoms or symptom-free for three days, whichever was longer. The parents were instructed to remain the sole caregivers of the baby given reports of prolonged viral shedding in the stool of infants [4–6].

Discussion

To our knowledge, this was the first hospitalized young infant with SARS-CoV-2 in the state of California. While more data is emerging, the clinical presentation and illness course of COVID-19 infection in infants and children still remains poorly characterized. In contrast to the parents, who presented with the common symptoms in adult patients of fevers, coryza, myalgias, anosmia, and ageusia [7], our patient initially presented only with fever. Other previously reported symptoms in pediatric patients, such as pharyngeal erythema, diarrhea, and vomiting [8] were not observed. The patient developed a mild cough, and together with fever, these are the two most commonly reported symptoms in pediatric patients [8–11]. The patient's resolution of fever within 30 hours is consistent with other reports demonstrating that fever and mild respiratory symptoms may resolve within 24 hours of onset in young children [9]. Due to the mild symptomatology and possible longer

incubation time in children than adults, an exposure history in one or more affected family members is often the impetus for testing pediatric patients for SARS-CoV-2 infection [9,12].

The febrile infant 29-60 days-old is a common pediatric presentation in EDs, urgent care centers, and inpatient wards across the United States. In this case, the patient was hospitalized due to fever without localizing symptoms and pan-leukocytopenia in the setting of higher-risk anatomy for urinary tract infections. While the incidence is unclear, leukopenia, lymphopenia, and neutropenia have been reported in pediatric patients with COVID-19 [13], and presence of these lab findings should raise suspicion for a workup for the virus. Others have reported that procalcitonin is sometimes elevated in pediatric patients with COVID-19 [10], but this test was not sent for this infant. While our patient had a short hospitalization and good clinical outcome, there are subpopulations of children who may be at higher risk for complications [2]. Our case illustrates that the differential diagnosis for an infant with fever without a source should include COVID-19, as fever may be the only presenting symptom. Obtaining a thorough history for significant exposures may be useful, but often there are no known exposures.

As a result of our experience with this infant and expanded testing capabilities with regional adoption at KPNC of the Roche cobas 6800/8800 rRT-PCR for SARS-CoV-2, a number of practice changes were made. Prior to this case, there were no SARS-CoV-2 guidelines for testing young infants presenting with fever without a source. As of March 26, 2020, regionally all febrile infants under 2 months of age requiring hospitalization at KPNC will be tested for SARS-CoV-2. Personal protective equipment for contact and droplet precautions with eye protection (e.g. simple masks, eye shields, gloves and gowns) will be required for healthcare providers seeing febrile infants under 2 months of age to reduce healthcare related exposures while SARS-CoV-2 testing is pending.

In summary, we believe the main learning point of this case is that COVID-19 should be considered in the differential diagnosis for the young infant presenting with fever without a source. Healthcare institutions should set guidelines to ensure that proper protective equipment is provided to medical personnel to avoid exposure to healthcare workers while the diagnostic process is ongoing. In the setting of limited testing and access to protective equipment, national discussions are required to strike the right balance between identifying at-risk pediatric populations while conserving resources. Parents of SARS-CoV-2-positive children should be counseled on methods to avoid further community spread of the virus.

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