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

Table of Contents Summary

This study describes clinical presentations of three febrile infants less than two months of age hospitalized in a New York pediatric hospital.

Contributors' Statement Page

Drs. Feld, Belfer and Kabra conceptualized and designed the study, collected data, drafted the initial manuscript, obtained consents, and reviewed and revised the manuscript.
Drs. Rai and Moriarty collected data, and reviewed and revised the manuscript.
Dr. Goenka collected data, revised the manuscript, and critically reviewed the manuscript for important intellectual content.
Dr. Barone supervised data collection, revised the manuscript, and critically reviewed the manuscript for important intellectual content.
All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Abstract

We describe three febrile infants less than two months of age admitted to a large, tertiary care children's hospital in New York and subsequently found to be infected with SARS-CoV-2. All three patients presented with fever, feeding difficulty, lymphopenia, and thrombocytosis on laboratory evaluation. Two of the three patients were found to have neutropenia and two had known exposures to sick contacts. This case series describes three of the youngest patients to be reported with SARS-CoV-2 in the United States.

Introduction

The 2019 novel coronavirus (SARS-CoV-2) has spread rapidly across the globe since it was identified in January 2020. Pediatric cases have been described in China,[1,2,3,4] but the clinical characteristics of pediatric patients affected in the United States are only being described. The few published studies in this population report milder cases, although the reason for this is unknown.[5,6] Literature which describes the epidemiology, clinical features and prognosis of SARS-CoV-2 in neonates and infants is scarce. One study suggests infants, although rarely affected, are vulnerable to severe manifestations.[1] As the number of pediatric cases in the US continues to climb, there is opportunity to further describe neonatal and infantile presentations of SARS-CoV-2. Here, we describe three hospitalized infants less than two months of age who presented to a large tertiary-care pediatric hospital and were found to be infected with SARS-CoV-2.

Patient 1

A 43-day-old full term previously healthy male presented to the pediatric emergency department (PED) on March 17, 2020 with the chief complaint of fever and lethargy for one day. Two days prior, the infant developed nasal congestion. There was no report of cough, difficulty breathing, or gastrointestinal symptoms. The mother of the child reported difficulty feeding that

was attributed to the infant's lethargy. A rectal temperature taken at home was noted to be 39.2 ºC. Emergency medical services were called, and the infant was brought to the PED.

Of note, the infant's parents and uncle had recently attended a wedding with an individual suspected to be infected with SARS-CoV-2. At the time of the infant's presentation, SARS-CoV-2 testing of multiple family members was pending. Upon presentation to the PED, the patient was febrile to 38.2 ºC with normal oxygen saturation. The patient was noted to be lethargic, markedly irritable, and had nasal congestion. The rest of his exam was unremarkable.

Blood, urine and cerebrospinal fluid (CSF) cultures were obtained with routine hematological, urine and CSF studies; results are listed in Table 1. The patient was noted to have lymphopenia, neutropenia and thrombocytosis. Additionally, the patient had a negative respiratory viral panel (RVP) and a negative CSF PCR panel. SARS-CoV-2 testing was obtained due to the family's suspected exposure. The patient was admitted and antibiotics were initiated. Blood, urine and CSF cultures were ultimately negative, and the SARS-CoV-2 PCR was positive. On day two of admission, the patient developed mild respiratory distress with tachypnea and subcostal retractions. He did not require any additional respiratory support. The patient was discharged, without complications, on day three of admission.

Patient 2

A 28-day-old male, born at 36 weeks gestation, presented to the PED on March 20, 2020 with the chief complaint of fever, sleepiness and poor feeding for one day. The patient had no associated cough, nasal congestion, rhinorrhea or gastrointestinal symptoms. A rectal temperature was taken at home and noted to be 38.8 ºC. There were no known sick contacts or any known SARS-CoV-2 exposure.

Upon presentation to the PED, the patient was febrile to 38.5 ºC with a normal oxygen saturation. The patient was noted to be lethargic but arousable, with mottled skin and prolonged capillary refill. The respiratory exam was unremarkable. Blood, urine and CSF cultures were obtained along with routine hematological, urine and CSF studies; results are listed in Table 1. The initial laboratory studies were notable for lymphopenia and thrombocytosis. The patient had a negative RVP. The patient was admitted and antibiotics initiated. The clinical decision to test for SARS-CoV-2 was made due to persistent irritability and lymphopenia. Blood, urine and CSF cultures were negative. The SARS-CoV-2 PCR was positive on day one of admission. The patient was discharged, without complications on day two of admission.

Patient 3

A 43-day-old full term female with a solitary left-sided kidney presented to the PED on March 20, 2020 with fever. Concerned that the baby felt warm at home, the parents took a rectal temperature that was noted to be 38 ºC. The patient had been feeding well at home without evidence of respiratory distress. The father of the patient, who was a physician, had tested positive for the SARS-CoV-2 virus on the day of the patient's presentation.

Upon presentation to the PED, the patient was afebrile with a normal oxygen saturation. The patient was noted to be well-appearing with an unremarkable physical exam. An evaluation of routine hematological and urine studies was undertaken. The hematologic laboratory findings were notable for lymphopenia, neutropenia and thrombocytosis; results are listed in Table 1. The patient had a negative RVP and no CSF studies were obtained. The infant was tested for SARS-CoV-2 due to the known infected family contact. The patient was discharged from the PED without concern for a serious bacterial infection.

The following day the patient's SARS-CoV-2 PCR was noted to be positive. The patient was called back to the PED because of a positive blood culture for *streptococcus salivarius*. On return to the PED, physical exam was again unremarkable. A repeat blood culture was obtained and the patient was admitted. He was discharged following a negative repeat blood culture result. The initial positive blood culture was deemed to be a contaminant.

Discussion

This case series describes three of the youngest pediatric patients reported to date with SARS-CoV-2 infection. Data on the characteristics and clinical features of children with the 2019 novel coronavirus (SARS-CoV-2) is beginning to be published based on the experience in China, but very little has been published from the United States. Additionally, little is known thus far about the effect of SARS-CoV-2 on infants.

The Chinese Center for Disease Control and Prevention reported that only 1% (416 cases) of 72,314 confirmed or suspected cases were in children <10 years of age.[2] There were no deaths reported. Dong and his colleagues presented a review of 2143 pediatric patients in China with confirmed or suspected cases of SARS-CoV-2, with 17.7% of them in children less than one year of age.[1] Additional data on infected children at Wuhan Children's Hospital mirrors this, with 31 of 171 infected children (18.1%) less than one year of age.[7]

Less is known about the clinical course of infected infants with SARS-CoV-2. Wei, et al reported only nine hospitalized infants diagnosed with SARS-CoV-2 between December 8, 2019, and February 6, 2020 in China. The patients ranged in age from one month to 11 months, and all nine infants had at least one infected family member. The authors did not fully describe the patients' hospital courses, but four had fever on presentation and two had mild upper respiratory tract symptoms. None of the nine infants had severe complications or required critical care

management.[3] Cai, et al described a series of 10 children infected with the virus, two of these patients under 12 months of age, with little information published about the severity of illness.[8]

There have been reports of significant morbidity and mortality in infants with SARS-CoV-2. The review from Wuhan Children's Hospital describes the death of a 10-month-old child with intussusception who developed multiorgan failure and died four weeks after admission.[7] Cui, et al described a 55-day-old otherwise healthy female presenting with rhinorrhea and cough, with known SARS-CoV-2 exposure, who was admitted, tested positive, and subsequently developed liver and cardiac injury.[9] Published reports based on the experience of SARS-CoV-2 infection in infants in China suggest that the number of infected infants is small, and that the disease process in hospitalized patients is generally milder. Authors have speculated this may be from a lower risk of exposure or incomplete identification due to mild or asymptomatic disease.[3] This case series of three patients admitted to a children's hospital in New York over a period of one week in March suggests that the number of hospitalized infants with SARS-CoV-2 infection may ultimately be higher in the United States than in China. This series, while small, also suggests that in febrile infants without an otherwise identifiable source of illness on blood, urine, CSF, and RVP studies, SARS-CoV-2 should be considered as an etiology of the illness. All three patients described here presented with fever, feeding difficulty, and had an absence of cough. None of the three had respiratory distress, therefore no chest imaging was pursued. The three patients had lymphopenia and thrombocytosis on initial presentation, and two had neutropenia. All infants were tested via nasopharyngeal swab PCR testing. While two of the infants did have suspected or known SARS-CoV-2 exposure, hospital policy at the time of publication is to test all febrile patients without an obvious other source.

All three patients had unremarkable hospital courses. Two of the three patients required intravenous fluid support due to poor feeding. One patient had persistent tachycardia, attributed to irritability and dehydration. One of the three was discharged within 48 hours of admission, which is standard practice for our hospitalized febrile infants, and one patient remained an additional day due to his respiratory status. The third patient was admitted after being called back and was discharged under 36 hours later.

The clinical spectrum of SARS-CoV-2 infection is evolving. To date, much of the literature focuses on the respiratory sequelae of the illness. Our limited experience with hospitalized febrile infants with SARS-CoV-2 infection shows that while respiratory manifestations may be present, they are less prominent; irritability, lethargy, and poor feeding is more frequently encountered. Lymphopenia, thrombocytosis, and possibly neutropenia, in the absence of another fever source, may prompt investigation for SARS-CoV-2 infection. Further studies are needed to determine the impact of this rapidly emerging infection on the pediatric population.

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Table 1: Demographic and clinical characteristics of three infants with SARS-CoV-2.

	Patient 1	Patient 2	Patient 3
Patient Characteristics			
Age (days) at admission	43	28	43
Sex	Male	Male	Female
Exposure			
Contact with individual with confirmed SARS-CoV2 infection or individual with fever and/or respiratory symptoms	✔	✗	✔
Signs and symptoms			
Fever	✔	✔	✔
Cough	✗	✗	✗
Feeding difficulty	✔	✔	✔
Lethargy	✔	✔	✗
Irritability	✔	✔	✗
Supplemental oxygen support	✗	✗	✗
Laboratory Studies			
Leukocytes (K/uL)*	3.85 (6.0-17.5)	7.49 (5-19.5)	5.28 (6.0-17.5)
Neutrophils (K/uL)*	0.79 (1.5-8.5)	4.44 (1.0-9.0)	0.90 (1.5-8.5)
Lymphocytes (K/uL)*	1.82 (4.0-10.5)	1.62 (2.5-16.5)	2.65 (4.0-10.5)
Platelets (K/uL)	523	455	529

	(150-400)	(120-370)	(150-400)
CSF Leukocytes (cell/uL)	10	1	N/A
Hospital Course			
Respiratory distress	✔	✗	✗
Need for supplemental IV fluids	✔	✔	✗
Airborne isolation precautions	✔	✔	✔
Length of stay (hours)	92	45	**

*Age-appropriate reference ranges listed under each value

** Patient was not admitted on initial presentation

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