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A case series of pediatric croup with COVID-19

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ABSTRACT

We describe three previously healthy children, admitted from our emergency department (ED) to our free-standing children's hospital, as the first documented cases of croup as a manifestation of SARS-CoV-2 infection. All three cases (ages 11 months, 2 years, and 9 years old) presented with non-specific upper-respiratory-tract symptoms that developed into a barky cough with associated stridor at rest and respiratory distress. All were diagnosed with SARS-CoV-2 by polymerase chain reaction testing from nasopharyngeal samples that were negative for all other pathogens including the most common etiologies for croup. Each received multiple (≥3) doses of nebulized racemic epinephrine with minimal to no improvement shortly after medication. All had a prolonged period of time from ED presentation until the resolution of their stridor at rest (13, 19, and 21 h). All received dexamethasone early in their ED treatment and all were admitted. All three received at least one additional dose of dexamethasone, an atypical treatment occurrence in our hospital, due to each patient's prolonged duration of symptoms. One child required heliox therapy and admission to intensive care. All patients were eventually discharged. Pathogen testing is usually not indicated in croup, but with "COVID-19 croup," SARS-CoV-2 testing should be considered given the prognostic significance and prolonged quarantine implications. Our limited experience with this newly described COVID-19 croup condition suggests that cases can present with significant pathology and might not improve as rapidly as those with typical croup.

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1. Introduction

The novel 2019 coronavirus SARS-CoV-2, responsible for COVID-19 disease, commonly presents in children with fever, cough or shortness of breath [1-3]. Other findings can include rhinorrhea, nausea, vomiting, fatigue, diarrhea, dehydration, abdominal pain, headache, pharyngitis, rash, myalgia, cyanosis, tachypnea, tachycardia, apnea, and other presentations [1,3-5]. We are unaware of any reports of SARS-CoV-2 associated with stridor and croup.

Croup (laryngotracheitis) is usually caused by viral infections (most commonly parainfluenza types 1 to 3) in the fall and winter months [6]. Croup typically presents with a "barky cough" and in more severe cases may develop stridor and dyspnea [7]. After an electronic health record database review, we describe this case series of our ED's only three cases, between March 1, 2020 and July 31, 2020, of children who received nebulized racemic epinephrine (NRE) and had a positive SARS-CoV-2 infection.

2. Case reports

2.1. Case 1

In June, an 11-month-old previously healthy African-American male twin, with no sick contacts, presented with one day of cough, fever, and rhinorrhea. On ED arrival, he was febrile (104.9 °C), tachypneic (56/min), and had a 97% oxygen saturation. His exam at rest was notable for biphasic stridor, barky cough, moderate retractions, decreased aeration, and no wheeze. Oral dexamethasone (0.6 mg/kg) and NRE (0.5 mL of 2.25% in saline) were administered without improvement. A second NRE two hours later did not resolve the stridor and he was admitted. A nasopharyngeal respiratory pathogen PCR panel (BioFire® FilmArray® Respiratory RP2.1) was positive for SARS-CoV2 and negative for all other pathogens.

As an inpatient, he got a third NRE three hours after the second one, with no response. His stridor continued 21 h after the initial dexamethasone. As an inpatient, he received a second oral dexamethasone (0.6 mg/kg), 24 h after the first dose, an infrequent occurrence on the

Abbreviations: BiPAP, Bilevel Positive Airway Pressure; COVID-19, coronavirus disease of 2019; ED, Emergency Department; IV, intravenous; mg/kg, milligrams per kilogram; NRE, nebulized racemic epinephrine; pCO2, partial pressure of carbon dioxide; PCR, polymerase chain reaction; PICU, pediatric intensive care unit; SARS-CoV-2, Severe Acute Respiratory Syndrome coronavirus 2.

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inpatient service for croup. He was discharged after 32 h of hospitalization. At discharge, he had stridor with exertion only. On phone follow-up, the mother reported that "his breathing got much better the day after he was discharged."

2.2. Case 2

In June, a 2-year-old previously healthy Caucasian female presented with two days of cough and dyspnea without fever. She had two prior episodes of stridor with upper-respiratory tract infections. The day prior, a telehealth physician diagnosed her with an upper-respiratory tract infection. Her father and sister both had fever but had not had SARS-CoV-2 testing.

On ED arrival, she was afebrile (37.0 °C), tachycardic (144/min), tachypneic (44/min), and had a 99% oxygen saturation. She had stridor at rest with moderate retractions, barky cough, decreased aeration, no wheeze, a normal cardiac exam, and a blanching maculopapular truncal rash. Oral dexamethasone (0.6 mg/kg) and NRE were administered. A second NRE was given fifty minutes later for persistent stridor and retractions. Two-view neck radiographs revealed mild subglottic narrowing with no radiopaque foreign body. Chest radiographs were normal. Her nasopharyngeal PCR panel was also positive for an isolated SARS-CoV2 infection.

She was admitted and was treated with a third NRE for persistent stridor, 2.5 h after the previous one, with no response. Otorhinolaryngology was consulted for persistent stridor and ultimately recommended dexamethasone (0.6 mg/kg) every 6 h for 24 h for severe croup. She had stridor at rest for 13 h after the first dexamethasone and was discharged 17 h after admission with stridor only with exertion. On follow-up, the mother reported improved symptoms within one week, but two months later has noted that her daughter "gets winded easily" and is "not back at full capacity."

2.3. Case 3

In July, a 9-year-old previously healthy female presented as a transfer from an outside ED with a complaint of coughing. Her mother had tested positive for COVID-19 ten days before presentation, and the patient's symptoms started three days after her mother's test. Her pediatrician advised the family to seek ED care only if she developed respiratory distress. On day six of illness, the coughing became barky without any improvement with dextromethorphan-acetaminophen-doxylamine succinate, so she presented to an adult ED. She was febrile (100.5° F), tachypneic (42 breaths/min) and had a 95% oxygen saturation. For her respiratory distress and inspiratory stridor at rest, she was given racemic epinephrine, codeine, and lorazepam. Two hours later, she was speaking in full sentences and breathing at 28 breaths/min. After a normal chest radiograph, and a nasopharyngeal viral PCR panel that was positive only for SARS-CoV-2, she was discharged.

Twelve hours later, she returned to the same ED with "continuous barky coughing," tachypnea (56 breaths/min), inspiratory stridor at rest, and an oxygen saturation of 94%. A repeat chest radiograph showed "subtle patchy opacities in both lower lobes may represent early pneumonia" which was treated with ceftriaxone. She received nebulized normal saline and four puffs of an albuterol inhaler with no response. The ED physician consulted us and we recommended NRE and dexamethasone. A complete metabolic panel and complete blood count was unremarkable with a C reactive protein of 1.8 mg/deciliter. En route by ambulance, she received her third NRE with no response.

On arrival to our ED, she had a heart rate of 150/min, respiratory rate of 34/min, blood pressure of 125/72, and an oxygen saturation of 98%. She was air-hungry, diaphoretic, spoke in a hoarse whisper, separated by back-to-back barky coughs every minute, and complained of chest pain with coughing. Her exam revealed severe work of breathing, inspiratory stridor at rest, poor aeration, and no wheeze. Her venous blood gas had a pH of 7.43 with a pCO2 of 34. A fourth NRE made her distress worse. Next, BiPAP was trialed but she could not tolerate it. A two-minute trial of prone positioning also failed. A three-minute trial of heliox (70% helium/30% oxygen) was given with no improvement and was discontinued. The patient was transported to the pediatric intensive care unit (PICU) on oxygen by non-rebreather mask with intubation equipment if needed.

In the PICU, another BiPAP trial failed and the patient was given IV midazolam (0.05 mg/kg) for anxiolysis. Heliox was trialed again as a last attempt before intubation. Her respiratory effort slowly improved on heliox which she received for 22 h along with a dexmedetomidine infusion. Her tachypnea resolved after four hours on heliox and her stridor at rest lasted for 19 h after the initial dexamethasone. She was started on dexamethasone (0.25 mg/kg) IV every 6 h for 48 h and switched to oral dosing for 24 h. Remdesivir IV was given for five days. Repeat chest radiographs showed no pneumonia and she received no further antibiotics. Over four days in the PICU, she received intermittent heliox and benzodiazepines to treat her air hunger and respiratory distress. She was discharged after one additional day on the inpatient service. Her mother noted that she was "fully recovered" from all symptoms one week after discharge.

3. Discussion

This case series describes the first three cases, to our knowledge, of isolated SARS-CoV-2 infection with pediatric croup. All three were tested with PCR-based pathogen panels that screened for the most common etiologies of croup [8]. In most clinical circumstances, determining the etiology of croup is rarely helpful [8]. In this current pandemic, however, identifying if pediatric croup is associated with SARS-CoV-2 infection assumes novel importance for counseling inpatient and outpatient families on quarantine and home isolation precautions [9]. Given that historical peak incidence of croup is in the upcoming fall and winter months, these cases highlight the importance of inpatient and outpatient access to rapid SARS-CoV-2 testing [10]. Medical advice was sought before ED care in two of these described cases, underscoring the importance of good anticipatory guidance for seeking acute care. Their course of acute care was atypical in severity, with potential implications for the expected natural history and management of future cases. There might have been additional cases of COVID-19 croup without stridor, who did not require racemic epinephrine, in our ED. These cases were not included in our electronic health record query due to our local practice standard of not testing most patients who meet discharge criteria for viral etiologies such as SARS-CoV-2 infection. Given the quarantine implications of discovering SARS-CoV-2 infection in children, regardless of their clinical severity, our local testing practices have changed to now test all croup patients for SARS-CoV-2.

All three of the described COVID-19 croup patients had stridor at rest which was relatively unresponsive to multiple NRE treatments. NRE reduces croup symptom scores by decreasing upper airway edema, a finding that might be commonly seen with COVID-19 pathophysiology [11-14]. While this case series is limited to only three patients, all had ≥3 total NRE treatments, dexamethasone, and additional inpatient interventions (i.e., additional NRE, BiPAP, or heliox). Inpatient interventions for croup are relatively infrequent (22.6% in one study), suggesting potentially more severe pathophysiology with COVID-19 croup versus previously described croup [15]. Pediatric croup patients who received ≥3 NRE in one children's hospital were more likely to need intensive care management [16]. The receipt of NRE in COVID-19 croup patients also introduce concerns given the aerosol-generating nature of the procedure and the required personal protective equipment needs [17].

Dexamethasone is used in croup as it improves symptoms, decreases hospital length of stay, and reduces return visit rates [18]. All three cases received multiple doses of dexamethasone, a therapeutic decision that is infrequent for our hospital's practice and is reserved for atypical cases not responding as expected to initial treatments [19]. Symptom scores with dexamethasone typically improve in 0.5 to 4 h [18,20].

While we did not have longitudinal croup symptom scores (e.g., Westley scores), the time from initial dexamethasone to the resolution of stridor at rest ranged from 13 to 21 h [21]. This is significantly longer than our normal expectations for moderate to severe croup. Current COVID-19 guidelines recommend dexamethasone for adults who are mechanically ventilated or require oxygen [22,23]. Further study is warranted to determine effective steroid recommendations for pediatric COVID-19 croup patients.

4. Conclusion

New COVID-19 clinical presentations are emerging rapidly, outpaced "only by the transmission of the virus itself." [24] Our limited experience with this newly described COVID-19 croup suggests that cases can present with severe pathology and might not improve as rapidly with treatments as in typical croup patients. Testing for SARS-CoV-2 in pediatric croup assumes novel importance during this pandemic for both prognostic and quarantine implications. Further investigations are needed to determine the natural history and optimal management of COVID-19 croup.

Contributor Credit Author Statement

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Patient consent from parents was obtained from all three cases in this case series. In addition, parents have reviewed the reports for accuracy and have provided verbatim follow-up outcome quotes in descriptions of each case.

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Declarations of Competing Interest

None.

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