



Case report

Management of COVID-19 in an adolescent demonstrates lasting effects of extreme prematurity on pulmonary function

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ABSTRACT

Extremely premature infants have demonstrated increased survival due to advancements in care. This population is at risk for decreased lung function that persists into adolescence. It is important for clinicians to consider this history when treating and assessing such patients who contract SARS-CoV-2 respiratory infection.

A 17-year-old, former premature infant of 23 weeks gestation with BPD presented to the pediatric emergency department for evaluation of hypoxia and increased work of breathing in the setting of SARS-CoV-2 infection. He was managed aggressively with early noninvasive respiratory support, Remdesivir, systemic steroids, and convalescent plasma.

Utilization of aggressive medical therapies early in the hospital course assisted in preventing intubation and mechanical ventilation for this patient. While there are studies examining the severity of SARS-CoV-2 infection in premature infants, there is a paucity of data on this vulnerable group as they age into adolescence. More studies are needed to assess the severity of illness and optimal management of this population.

1. Introduction

Advances in neonatology have increased the survival of extremely premature infants, and infants with bronchopulmonary dysplasia (BPD) [1]. These infants have reduced lung function into their adolescent years, with a known decline in function that persists into adulthood [2, 3] making this vulnerable population one that can be significantly affected in the COVID-19 pandemic. There are few studies examining the outcomes of former extremely premature infants with SARS-CoV-2 respiratory infection, who have the potential to become seriously ill with respiratory infections [4]. The following case is a 17-year-old who was born at 23 weeks gestation and presented with hypoxia and respiratory distress due to SARS-CoV-2 infection. This case serves as a reminder to providers that prematurity and BPD are important historical risk factors in assessing the severity of respiratory infections including the current pandemic, even into adolescence. The use of noninvasive respiratory support helped bridge the patient to recovery as his medical treatment

began to take effect. His medical management was adapted from adult protocols, and represents a promising outcome for adolescents.

1.1. Case summary

A 17-year-old Hispanic male with asthma, prematurity born at 23 weeks, BPD, and autism was admitted to the pediatric intensive care unit due to acute hypoxic respiratory failure in the setting of SARS-CoV-2 associated pneumonia. His father was a positive contact and was admitted to the medical ICU prior to this patient's admission. The patient tested positive for SARS-CoV-2 PCR eight days prior to his admission. At that time the patient had developed isolated fevers with a peak temperature of 39.9 °C, but was otherwise asymptomatic. His home management included acetaminophen, and combination acetaminophen, dextromethorphan and phenylephrine. Six days after his positive test, he presented to the pediatric emergency department (PED) for shortness of breath. At that time, he did not have hypoxia, but did have

Abbreviations: Bronchopulmonary Dysplasia, (BPD); Bilevel Positive Airway Pressure, (BiPAP); Continuous Positive Airway Pressure, (CPAP); Coronavirus Disease, (COVID-19); High Flow Nasal Cannula, (HFNC); Intensive Care Unit, (ICU); (Polymerase Chain Reaction), PCR; Pediatric Intensive Care Unit, (PICU); Pediatric Emergency Department, (PED); Noninvasive Positive Pressure Ventilation, (NIPPV).

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laboratory criteria consistent with acute SARS-CoV-2 infection: lymphopenia and elevated c-reactive protein, in addition to a known positive PCR test. He had a chest x-ray at that time which showed mild bronchial wall thickening. He was otherwise medically stable and was discharged home. He returned to the PED two days later presenting with fever and hypoxia, room air O₂ saturations of 90%. His chest x-ray was notable for low lung volumes with bibasilar opacities. Laboratory abnormalities included an elevated lactic acid of 4.84 mmol/L, elevated c-reactive protein of 41.6 mg/L, and lymphopenia to absolute count of $0.9 \times 10^3/\mu\text{L}$. D-dimer, brain natriuretic peptide, troponin I, prothrombin time, partial prothrombin time and international normalized ratio were all normal. In the emergency department inhaled albuterol and ipratropium were delivered for symptomatic relief with no effect. The patient was admitted on respiratory support of 3 liters per minute oxygen via nasal cannula, but due to increased work of breathing, was quickly escalated to high-flow nasal cannula (HFNC) oxygen at 20 L per minute with 40% FiO₂, and subsequently escalated to biphasic positive pressure ventilation (BiPAP) (maximum settings RR 16, IPAP 12, EPAP 6, FiO₂ 0.6) using full face mask. On admission he received a 200mg loading dose of Remdesivir, which he continued at a dose of 100mg daily for five days. On hospital day one he received his first dose of convalescent plasma, and received daily for a total of six doses during his admission. He was also started on dexamethasone 6 mg daily for a ten-day course, or until hospital discharge. He was compliant with awake prone positioning for more than 12 hours daily. On hospital day three he weaned from BiPAP to HFNC and on hospital day six he was transitioned to low flow nasal cannula oxygen. On hospital day seven he weaned to room air, and on hospital day eight he was discharged home with no O₂ requirement.

2. Discussion

This patient had a prolonged course of illness, with severity peaking late in its course, ten days after his first fever and positive test. Most children with SARS-CoV-2 infection develop only a mild illness, and represent a small portion of the total population who become infected with this virus. There is limited evidence to show which comorbidities in children are associated with severe disease due to infection with SARS-CoV-2 [5]. In this patient, it is less likely that asthma played a significant role in the severity of his illness. Typical asthma treatments did not improve the patient's symptoms, and there is conflicting evidence on whether childhood asthma is truly a risk factor for development of severe respiratory disease in SARS-CoV-2. Although respiratory viruses are a common trigger of asthma exacerbations, similarly to this case, SARS-CoV-2 does not seem to trigger asthma exacerbations. In fact, it is suggested that, paradoxically, allergic asthma is a protective measure against severe disease due to potential under-expression of angiotensin-converting enzyme 2 (ACE2) receptor, which is required for coronavirus recognition and infection [7]. Previous studies have suggested that former premature individuals may have a more severe course of disease due to baseline ACE-2 overexpression; the main receptor in SARS-CoV-2 viral binding [8]. However, it is worth noting our patient had been using inhaled fluticasone, a steroid, which may have contributed to down-regulation of ACE-2 receptors [9].

Infants with BPD who have contracted SARS-CoV-2 have been reported in the literature and have a varying severity of acute illness ranging from management at home to pediatric ICU admission [6], however to date there are no studies of adolescents with history of BPD and acute respiratory illness. Given the severity of this patient's case, an important factor to consider is this patient's history of BPD. Previous studies have demonstrated that adolescents with a history of BPD have decreased Forced Expiratory Volume in 1 second (FEV₁), and that obstruction persists into adolescence [2,3]. This patient had mild obstruction on pulmonary function testing, from March 2020, with an FEV₁ to Forced Vital Capacity (FVC) ratio at 69%. His FEV₁ was 89% predicted. It is logical to consider that as these infants grow and develop,

they are likely at a higher risk of severe complications from SARS-CoV-2 due to the known reduction in their respiratory function.

Management of this patient's illness is notable for prone positioning, noninvasive respiratory support, and medical therapy. Although there is a risk of aerosolization with noninvasive respiratory support, this risk may be reduced by using lower pressures and a closed circuit. In this patient's case, a closed circuit was not utilized, however, a viral filter was placed over the exhalation port of the high-flow and BiPAP units. Additionally, the highest flow the patient received during his admission was 40 L per minute; below the limit set by the institution of 50 L per minute. Young adults with a similar history should be identified and clinicians should have a low threshold for PICU admission, as this population has the potential to decompensate quickly and require more advanced forms of respiratory support. This population may represent a group that benefits greatly with aggressive medical therapies. This patient received three key medical therapies to improve his respiratory status; a systemic steroid (dexamethasone), an antiviral medication (Remdesivir), and the study treatment convalescent plasma from patients who had previously recovered from SARS-COV-2 infection. Recent studies have shown convalescent plasma increases neutralizing antibody titers and reduces overall mortality in critically ill patients [9]. The use of remdesivir in pediatric patients has increased, as more children are presenting with severe disease [10]. In many cases the medication is used with improved clinical outcome and minimal side effects, in the short term [11]. The use of dexamethasone is a known treatment for adults with SARS-CoV-2 infection that reduces mortality in patients with severe disease [12]. Although the safety and efficacy of use of steroids in Pediatric patients infected with SARS-CoV-2 is not known, it is considered a reasonable therapy in children with more severe disease. [13,14].

Treatment options in the setting of more severe disease may include some combination of corticosteroids, antiviral therapies, and if available, convalescent plasma. Non-invasive positive pressure ventilation should be considered in this setting along with utilization of prone positioning protocols. Future studies may help better understand the effectiveness of these therapies individually in the pediatric population infected with SARS-CoV-2.

As more former premature infants age into adolescence and young adulthood during the current pandemic, an emphasis on historical factors is key to identify those who are at risk for respiratory decompensation. More studies are needed to compare former premature infants with BPD in their adolescent years to their full-term counterparts who developed SARS-CoV-2 infection and respiratory illness. This sentinel case serves as a reminder that BPD may be a risk factor for severe disease.

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Article summary

A former 23-week gestation infant, now an adolescent, contracted SARS-CoV-2 infection, representing an emerging population that should be considered in the current pandemic.

Declaration of competing interest

Have no conflicts of interest to disclose. There were no funding sources for this project.

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