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CASE REPORT

# Case Report: An Infant With Congenital Central Hypoventilation Syndrome And COVID-19

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## Abstract

To report a case of COVID-19 confirmed by PCR in a 10-month-old infant with central congenital hypoventilation syndrome, therefore dependent on mechanical ventilation. The main clinical features were fever, wheezing, prostration, and episodes of hypoxemia associated with hypercapnia. The patient received treatment with supplemental oxygen, in addition to antimicrobials for overlapping bacterial infection. Thirteen days after disease onset, the patient showed great improvement: supplemental oxygen was discontinued and mechanical ventilation parameters returned to baseline. Despite the underlying disease, the outcome was favorable. Discharge happened on the 17th day of disease and antimicrobial treatment was completed as outpatient.

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## INTRODUCTION

In December 2019, a growth in the number of cases of pneumonia of unknown cause was reported in Wuhan (China), involving particularly individuals who had visited a local seafood market. The virus was identified and the first death by the emerging disease recorded in early January 2020.[1] On March 11, the World Health Organization described the disease caused by SARS-CoV-2 - COVID-19 - a pandemic.[2] On June 26, 2020, Brazil ranked second in number of cases of the disease and deaths in the world.[3]

In Brazil, 1,316,667 cases and 57,070 deaths by COVID-19 had been recorded by June 27, 2020. By the end of Epidemiological Week 26 (June 21-27, 2020), 332,423 cases of severe acute respiratory syndrome (SARS) had been reported, 44.7% of which linked to COVID-19. Of these cases, 884 involved children aged less than one year, 729 involved children aged 1-5 years, and 1,544 involved subjects aged 6-19 years, which combined accounted for 2.1% of the population in question. The proportion of deaths by SARS associated with COVID-19 of individuals in the pediatric age range was even lower: 0.72%.[4] The data presented above reiterate the findings of recent systematic reviews about the progression of COVID-19 in children: the prevalence of critical/severe disease is below 6% and less than 1% are killed by the disease[5-7]. In adults, certain comorbidities have been established as risk factors for severe involvement. Similar comprehensive studies about the pediatric population featuring the quantification of comorbidities and their relationship with COVID-19 severity are still lacking.[5,8]

Therefore, reporting pediatric cases of COVID-19 – and specifically the ones in which comorbidities are present – becomes a relevant effort in the assessment of clinical progression and the identification of underlying conditions that might significantly affect patient outcomes.

## CASE REPORT

The patient described in this case is a female preterm infant aged 10 months, born after 34 weeks of gestation, dependent on mechanical ventilation via tracheostomy for congenital central hypoventilation syndrome (also known as Ondine's curse, a condition related to a PHOX2B gene mutation), with distal tracheal stenosis (80% obstruction related to tracheostomy complications), an ostium secundum atrial septal defect (without hemodynamic repercussion), central hypothyroidism managed with hormone replacement therapy, with a feeding tube placed due to oropharyngeal dysphagia, and on phenobarbital after having two neonatal seizure episodes.

The patient has been hospitalized since birth (waiting for a place in the State-sponsored homecare service) and kept on controlled pressure ventilation (inspiratory pressure 26 mmHg; end expiratory pressure 6 mmHg; respiratory rate 22 mpm). She had a self-limited course of coryza lasting for a day, which prompted a request for an immunofluorescence assay for respiratory viruses that came back negative. Three days later an increase was seen in the amount of secretion in the tracheostomy site, along with episodic decreases in oxygen saturation levels (down to 87%), at which times the patient required supplemental oxygen. The tracheostomy was reviewed and no changes that might justify the findings were identified. On the second day the patient presented hyaline coryza, wheezing (without respiratory effort), and more frequent drops in oxygen saturation. Chest X-ray images revealed no alterations in relation to baseline conditions. In the evening of the third day, the patient had low-grade fever (37.9ºC).

On the fourth day, the patient had episodic fever (up to 38.2ºC) along with signs of prostration and hypoxemia, primarily in the evening (87-88%), which prompted the prescription of supplemental oxygen (flow rate up to 4L/min). Positive pressure ventilation with a bag valve mask was occasionally needed in longer periods of desaturation. Additional chest X-ray images and the following tests were ordered: C-reactive protein (4.1 mg/L); complete blood count (7930 leukocytes with 58.7% segmented, 10.6% monocytes, and 28.2% lymphocytes; platelets 119,000); and blood gas (pH 7.27; pCO2 69.9 mmHg; $HCO_3$ 31.7 mmol/L). Chest X-ray images were normal. Ventilation parameters were altered (inspiratory pressure 27 mmHg, expiratory pressure 5 mmHg and respiratory rate 25 mpm). A PCR test performed on a nasopharyngeal swab specimen came back positive for SARS-CoV-2, and the patient was placed in isolation. On the following day, the patient had fever (up to 38.8º). On the sixth day, the patient tolerated a decrease in the oxygen flow rate to 0.5 L/min. On the ninth day of disease, the patient had five episodes of diarrhea without other signs of disease or hemodynamic alterations.

Additional tests were ordered on the tenth day of disease: complete blood count 6710 leukocytes (without left shift), platelets 263,000; and C-reactive protein 2.2mg/L. Another set of chest X-ray images were ordered, since the patient had frequent drops in oxygen saturation and sub-febrile temperature spikes. Clinical signs and images showing right retrocardiac and perihilar opacity prompted the prescription of amoxicillin/clavulanic acid and azithromycin. The respiratory rate was increased to 28 mpm due to $CO_2$ retention ($pCO_2$ = 61 mmHg) picked up in blood gas tests. Control blood gas tests showed good response ($pCO_2$ = 41.7 mmHg). On the following day, the respiratory rate was decreased to 25 with control blood gas tests showing $pCO_2$ = 38.5 mmHg. On the same day, antimicrobial therapy was switched to ciprofloxacin and sulfamethoxazole-trimethoprim, as a tracheal secretion antibiogram listed *Klebsiella oxytoca*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*. On the thirteenth day, the patient tolerated the removal of $O_2$ (oxygen saturation of 98% in ambient air) and mechanical ventilation was reset to baseline parameters (inspiratory pressure = 25cm$H_2O$; end expiratory pressure = 5 cm$H_2O$; respiratory rate = 25 mpm). On the fourteenth day, the patient had a few episodes of diarrhea, which resolved spontaneously. On the sixteenth and

seventeenth days of disease, nasopharyngeal swab specimens PCR-tested for SARS-CoV-2 came back negative. The patient was discharged, sent home (now on the State-sponsored homecare service), and prescribed treatment for pneumonia in an outpatient setting (thus completing 14 days on the latest antimicrobial therapy prescribed).

## DISCUSSION

Although COVID-19 is less severe in children (compared to adults), pediatricians must be able to recognize symptoms and assess the severity of involvement in patients with the disease. To date, only one study looked into the severity of disease as a function of age and reported that infants are at greater risk of developing severe disease.[9]

Three systematic reviews described the primary clinical manifestations, the distribution of severity, and the findings derived from complementary tests. Studies unanimously describe fever and coughing as the most prevalent symptoms, observed in about half of the cases. Coryza and gastrointestinal symptoms are present in up to 20% and 12% of the patients, respectively. In terms of severity, most patients have mild to moderate disease (96%), whereas 3% have severe disease (with hypoxia, dyspnea or cyanosis). Only 1% of the patients develop critical disease (with severe acute respiratory syndrome, respiratory failure, shock, encephalopathy etc.). Complete blood count tests find similar proportions of leukocytosis, leukopenia, and lymphopenia (about 15%). Approximately a quarter of the patients have increased C-reactive protein levels. The most frequent alterations seen in imaging tests are ground-glass opacity and consolidation. The patient described in this report did not undergo computed tomography (CT) to verify the existence of ground-glass opacity, but consolidation was seen in chest X-ray images. We did not believe CT scans would add to the management of the patient; additionally, exposure to radiation should be avoided whenever possible[5-7,10]. A recent study on COVID-19 in children found that up to 65% of the patients are diagnosed with pneumonia, a less than surprising finding, since viral and bacterial coinfection is not rare in diseases of the lower respiratory tract.[11,12]

Although deaths are rare among children with COVID-19, it is important to mention that pediatric patients with preexisting severe conditions are at risk of dying[5-7]. In the case presented herein, the patient had been diagnosed with congenital central hypoventilation syndrome, an incurable disease related to a PHOX2B gene mutation, characterized by alveolar hypoventilation, hypoxemia, and hypercapnia, particularly during sleep. Proper management includes the optimization of ventilation and oxygenation with the aid of a mechanical ventilator, in order to minimize the chances of neurocognitive impairment and prevent hypoxemia, pulmonary hypertension, and cor pulmonale.[13]

## CONCLUSION

The infant described in this case had severe COVID-19. However, the fact that she had been hospitalized at the time of symptom onset - which permitted early diagnosis, ample monitoring, and timely start of therapy - probably spared her from developing critical disease.

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