

## COVID-19 in an adolescent with cerebral palsy: *A case report*

COVID-19 em um adolescente com paralisia cerebral: Um relato de caso

COVID-19 en un adolescente con parálisis cerebral: Informe de un caso

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### Abstract

**Background:** Children have been impacted by COVID-19 pandemics and biological mechanisms of host response are under active investigation worldwide to develop better treatment plans. Children with cerebral palsy (CP) diagnosis are less studied, although they present increased risk for COVID-19 disease (COVID-CP). Here, we aim to report the diagnosis and treatment plan to further improve clinical protocols for COVID-CP patients. **Case Presentation:** This case report describes a 12-year-old male diagnosed with neuropsychomotor developmental delay, chronic non-progressive encephalopathy, spastic tetraparesis, epilepsy and recently COVID-19 disease. SARS-CoV-2 viral detection was assayed by RT-PCR swab (nasopharynx and oropharynx) concomitantly with family members. Subject presented symptoms after 3 days of confirmed diagnostics and presented positive viral even after 2 weeks of testing, suggesting long exposure to the virus. The unique signs and symptoms led the treatment plan to focus on maintaining oxygen levels, management of severe lung phenotype, and control of increased seizures. In addition, levels of inflammatory cytokines were monitored to predict risk of cytokine storm, risk for multisystemic inflammatory syndrome (MISC), and need for continuous hospitalization. A pharmacological treatment protocol for asthma was implemented in association to vigorous monitoring by caregivers and family members. The course of the viral phase, from its onset to negativity, was longer than the average time of 14 days. **Conclusion:** Clinical manifestations, complementary exams and treatment are discussed to better improve protocols of COVID-CP patients.

**Keywords:** Cerebral palsy; Covid-19; Epilepsy; Cytokines; Continuous positive airway pressure; Case reports.

### Resumo

**Introdução:** Crianças são afetadas por pandemias de COVID-19 e os mecanismos biológicos de resposta do hospedeiro estão sob investigação em todo o mundo. Crianças com diagnóstico de paralisia cerebral (PC) são menos estudadas, embora apresentem risco aumentado para doença COVID-19 (COVID-PC). O objetivo é relatar o diagnóstico e plano de tratamento para melhorar ainda mais os protocolos clínicos para pacientes com COVID-PC. **Apresentação do caso:** Descreve-se um relato de caso de um adolescente de 12 anos com diagnóstico de atraso no desenvolvimento neuropsicomotor, encefalopatia crônica não progressiva, tetraparesia espástica, epilepsia e COVID-19. A detecção do vírus SARS-CoV-2 foi avaliada por swab de RT-PCR (nasofaringe e orofaringe) concomitantemente com membros da família. Ele apresentou sintomas após 3 dias do diagnóstico e apresentou vírus positivo após 2 semanas de teste, sugerindo longa exposição ao vírus. Os sinais e sintomas únicos levaram a se concentrarem na manutenção dos níveis de oxigênio, no manejo do fenótipo pulmonar grave e no controle do aumento das convulsões. Além disso, os níveis de citocinas inflamatórias foram monitorados para prever o risco de tempestade de citocinas, risco de síndrome inflamatória multissistêmica (MISC) e necessidade de hospitalização contínua. Um protocolo de tratamento farmacológico para asma foi implementado em associação ao monitoramento vigoroso por cuidadores e familiares. O curso da fase viral, do início

à negatividade, foi mais longo do que o tempo médio de 14 dias. Conclusão: As manifestações clínicas, exames complementares e tratamento são discutidos para melhor aprimorar os protocolos dos pacientes com COVID-PC.

**Palavras-chave:** Paralisia cerebral; Covid-19; Epilepsia; Citocinas; Pressão positiva nas vias aéreas; Relatos de casos.

### Resumen

Introducción: los niños son afectados por la pandemia de COVID-19 y los mecanismos biológicos de la respuesta inmunológica son investigados en todo el mundo. Los niños con parálisis cerebral (PC) son menos estudiados, aunque presentan un mayor riesgo de enfermedad COVID-19 (COVID-PC). El objetivo de estudio es informar el diagnóstico y tratamiento para mejorar los protocolos clínicos de estos pacientes. Presentación del caso: Este informe de caso describe un niño de 12 años diagnosticado con retraso del desarrollo neuropsicomotor, encefalopatía crónica no progresiva, tetraparesia espástica, epilepsia y COVID-19. La detección del SARS-CoV-2 se analizó mediante un hisopo RT-PCR (nasofaringe y orofaringe) concomitantemente con parientes. Él presentó síntomas después de 3 días de diagnóstico confirmado y virus positivo después de 2 semanas de prueba, sugiriendo una exposición prolongada al virus. Los signos y síntomas únicos llevaron a centrarse en mantener los niveles de oxígeno, el manejo del fenotipo pulmonar severo y el control del aumento de las convulsiones. Además, se controlaron los niveles de citocinas inflamatorias para reducir el riesgo de tormenta de citocinas, síndrome inflamatorio multisistémico (MISC) y la necesidad de hospitalización. Se implementó un protocolo de tratamiento farmacológico para el asma en asociación con un seguimiento riguroso por parte de los cuidadores y familiares. El curso de la fase viral, desde su inicio hasta la negatividad, fue más largo que el tiempo promedio de 14 días. Conclusión: Se discuten las manifestaciones clínicas, los exámenes complementarios y el tratamiento para mejorar los protocolos de los pacientes con COVID-PC.

**Palabras clave:** Parálisis cerebral; Covid-19; Epilepsia; Citocinas; Presión de las vías aéreas positiva continua; Informes de casos.

## 1. Introduction

Coronaviruses have been studied for more than 50 years, and recently SARS-COV-2 first emerged in Wuhan, December of 2019, prior to reaching populations globally. Characterized by a large range of clinical manifestations- i.e. fever, dry cough, headache, nausea, diarrhea, pneumonia, acute respiratory distress syndrome (Guan et al., 2020; Huang et al., 2020), this COVID-19 disease was named by the World Health Organization (WHO) and continues to impact adults and children worldwide. Investigations on pediatric population positive to SARS-CoV-2 infection have showed distinct responses when compared to adults, demonstrating higher frequency of asymptomatic and oligosymptomatic cases (Jiehao et al., 2020; Needleman & Hanson, 2020). Evidence suggests that pediatric subjects harbor higher amounts of the virus when compared to adults (Heald-Sargent et al., 2020) and present greater risk to infect family members. While COVID-19 in children is frequent, a recent systematic review (Mustafa & L, 2020) has shown that their clinical manifestations to be milder with better prognosis than adults with extremely low death rates (Szablewski et al., 2020; Wu & McGoogan, 2020). According to Centers for Disease Control (CDC, 2019a; CDC 2019b; CDC 2020) in contrast to asymptomatic cases, there are reports of children presenting severe signs and symptoms, with long-term consequences, a condition called MISC (Chen et al., 2020; Kabeerdoss et al., 2021).

Children with CP diagnosis are, however, less investigated than healthy pediatric patients. Due to biological and medical reasons, CP patients present a higher risk for COVID-19 disease (COVID-CP) and present needs and considerations important to the disease, including inability to wear mask, elevated seizure frequency, aberrant immune responses, presence of comorbidities, and continuous need of family supervision. Here, we aim to report the diagnosis and treatment plan to further improve clinical protocols for COVID-CP pediatric patients. We report treatment decisions for 12-year-old male teenager with neuropsychomotor developmental delay, chronic non-progressive encephalopathy, spastic tetraparesis and epilepsy diagnosed with Covid-19. Clinical manifestations, complementary exams and treatment plan are presented and discussed as COVID-CP patients are of special attention to during the pandemics.

## 2. Methodology

This case report was reviewed and approved by the Research Ethics Committee of the Cruzeiro do Sul University - Brazil Platform, São Paulo, Brazil (#37766720.9.0000.8084). Written informed consent was obtained from the patient's mother

after informed about the study.

Data related to diagnosis, disease history, exams, and drug and rehabilitation therapy were collected from records in the patient's medical record.

### 3. Case Presentation

The medical history of the 12-year-old Asian male teenager include cardiopulmonary arrest at 9 months-old due to hypoxia after obstruction of the airways by a foreign body. He was diagnosed with neuropsychomotor developmental delay, chronic non-progressive encephalopathy, spastic tetraparesis and epilepsy. Due to the presence of dysphagia he underwent a gastrotomy and it has been required, on average, approximately 50 oropharyngeal aspirations per day. In general, he has taken antiepileptic drugs (Levetiracetam, Lacosamide, Topiramate, Purodiol) frequently, but presents persistent convulsive crises (4 to 5 crises per day, lasting 5 to 10 minutes each).

Socially, the patient resides with his parents and maternal grandparents, which presented flu-like symptoms (i.e. headache, nasal congestion, running nose, and sore throat), and 3 days later they showed the signs of COVID-19 (fever, dry cough, tiredness, difficulty breathing, body pain and diarrhea). The patient's mother and grandparents were diagnosed with COVID-19 presenting positive oro- and nasopharynx swab for Sars-Cov-2. He manifested yellow secretions and higher fever that progressed to severe symptoms. The following day, a lab test was conducted to detect SARS-CoV-2 by RT-PCR swab (nasopharynx and oropharynx) which result was positive. He presented persistent fever of 102.2 Fahrenheit, which for 3 days, which was managed by paracetamol 500mg 1 tablet, 4 times a day.

Therapeutically, the patient is required to perform breathing exercises with Positive Airway Pressure (BIPAP), by employing 3 liters of oxygen twice a day in 3 series of 20 breaths each. At night, BIPAP is used continuously with a facemask from 12:00 to 04:00 am. Due to SARS-CoV-2 infection, a clinical consideration was taken by the pneumonologist to pause the BIPAP exercises, in order to prevent further cross-contamination in the household or caregivers. A protocol for asthma was administered to maintain oxygen levels (0.25 mg/ml of Budesonide nebulization twice a day for 7 days), inhalation prepared with 40 drops of Ipratropium bromide added to 5 ml of saline 3 times a day; 20 mg of Prednisone for 5 days and use of 2 liters of oxygen by nasal catheter maintaining oxygen saturation (SpO<sub>2</sub>) 100%). Thus, improving the patient's airway and oxygen levels, these levels were continuously monitored in the home settings.

In addition to conventional seizures (duration: 5 to 10 minutes), the patient presented 6 to 7 short seizures (duration: 40 seconds), with interval of 1 minute between each crisis, usually around 11 pm, with increased muscle tonus, lingual cyanosis, heart rate between 160 and 170 bpm and SpO<sub>2</sub>: 93 at rest, with a lethargic level of consciousness. These short and intense crises lasted for five continuous day, managed managed with the same prescribed antiepileptic drugs doses. These seizures have decreased after COVID-19 symptoms became moderate. Arterial systolic and diastolic pressure were 100mmHg and 60mmHg, respectively. No visible alterations were noted in chest X-ray. Other clinical features include bilateral auscultation with sparse respiratory auscultation of bilateral rhonchi; heart rate of 94bpm, SpO<sub>2</sub>: 97 and lethargic consciousness level. Patient was continuously monitored to observe levels of consciousness and breathing. Family was recommended to wear masks at all times, while COVID-CP patient did not due to risk of suffocation.

The hematology laboratory levels showed an increase in the number of platelets (494,000/uL) in the blood count, which might help to create thrombocyte adhesion, but no treatment was devised. An increase in the number of eosinophils (579/ $\mu$ L) was also noted, possibly associated with the presence of asthma developed during the contamination by SARS-CoV-2, which was treated with the same proposed protocol for asthma.

Other complementary exams presented results within the range of normality. To further investigate cytokine storm and the risk of MISC development, serum inflammatory cytokines were evaluated (interleukin-IL-6; IL10, Tumor Necrosis Factor-

TNF-  $\alpha$ . The patient's registered levels of inflammatory cytokines were IL -6 (1.5 pg/mL), IL-10 (inferior to 5.00 pg/mL), and TNF- $\alpha$  (5.47 pg/mL). Healthcare providers followed recommendations of Centers for Disease Control and Prevention (CDC, 2020) to keep the patient and parents and/or caregivers safe, and concluded this patient was not at risk to further develop severe disease.

A second RT-PCR test was performed after 15 days of the first positive exam. Patient showed positive to SARS-CoV-2 by RT-PCR (swab, nasopharynx and oropharynx), an only negative result was detected after the third test (15 days after the second exam). Thus, course of the viral phase of the disease, from its onset to negativity, was longer than the average time of 14 days. Informed consent in publishing this case was authorized and assigned by his parents and/or legal representative. Patient and family member have successfully recovered from COVID-19 without further damages.

#### 4. Discussion

Brain injury caused by hypoxia increases the risk of developing difficult-to-control epilepsy. In the presence of SARS-CoV-2 infection, there is a greater susceptibility to the occurrence of seizures, increasing the vulnerability of subjects due to homecare needs, and comorbidities, CP patients present inherent challenges during the daily routine and a constant treatment in the daily schedule for caregivers and family members. Respecting the simple safeguarding measures such as the use of masks and hand washing, and in many cases the use of the mask is inadvisable since they may be unable to remove the mask without assistance, and these patients are at increased risk of suffocation (Esposito & Principi, 2020; Fisher et al., 2020). There is no literature describing clinical manifestations and treatment of COVID-CP patients. In this case report, administering the medication for asthma control (prednisone) precociously (Dove et al., 2021; Shen et al., 2020) showed successful outcomes which might have been responsible for rapid remission of symptoms. The genomic mechanism of corticosteroids, as the prednisone used to control lung edema and inflammation of the patient of the case reported, is based in the action mediated via cytosolic glucocorticoid receptor (cGCR). Due to its lipophilic structure, corticosteroids pass through plasma membranes and bind to cGCR. The glucocorticoid-cGCR complex translocates to the cell's nucleus and binds to positive glucocorticoid response elements (GRE). Once binding to the positive GRE, the glucocorticoid-cGCR complex activates a transcription of anti-inflammatory proteins (such as IL-10, annexin 1, inhibitor of factor nuclear-kappa B (NF- $\kappa$ B), and others. Once binding to the negative GRE, the glucocorticoid-cGCR complex inhibits transcription of inflammatory transcription factor proteins (NF- $\kappa$ B) and activator protein-1 (AP-1), responsible for major anti-inflammatory and immunosuppressive effects due to the suppressed synthesis of pro-inflammatory cytokines- e.g IL-1, TNF $\alpha$ , interferon (IFN) $\gamma$ , and others (Rogatsky & Ivashkiv, 2006).

Due to comorbidities, children with CP present a large variation in clinical manifestations and severity. In addition, at home and/or hospital care, it is important to consider their oxygen levels, posture, seizure frequencies, consciousness and inflammatory levels. Gustatory and olfactory impairment was not observed in this patient, yet it is frequently associated with xerostomia (Fantozzi et al., 2020; Qiu et al., 2020).

The homecare was essential to prevent continuous family dissemination of COVID-19 and the success of establishing an early airway protocol, including asthma prescription, showed that the patient airways to be maintained. Due to excessive seizure episodes, it was critical for the survival of the patient to establish a monitoring protocol among the caregivers and family members (24 hours/day) to maintain health and prevent further damage. At this stage, it is unclear whether children are as susceptible to infection by SARS-COV-2 versus adults.

#### 5. Final Considerations

We reported clinical manifestations, complementary exams and treatment plan for a 12-year-old male teenager with

neuropsychomotor developmental delay, chronic non-progressive encephalopathy, spastic tetraparesis and epilepsy diagnosed with COVID-19. The authors signalize 3 important points:

1. Individuals with cerebral palsy are more prone to the occurrence of seizures, in the presence of SARS-CoV-2 infection;

2. Cerebral palsy condition increases risk of SARS-CoV-2 severe infection. In addition, the presence of comorbidities associated with cerebral palsy, such as epilepsy, and respiratory illnesses, contribute to the individual's host response impairment and vulnerability to develop severe infections, and;

3. COVID-CP subject's use of masks should be supervised or avoided, as they are at a greater risk of asthma and suffocation. A protocol to monitor and control lung inflammation and edema (such as prednisone) should be established to prevent severe lung phenotypes.

Literature and studies related to COVID-CP are scarce and new researches focused on it are necessary.

## Declarations

### Ethics approval and consent to participate

This case report was reviewed and approved by the Research Ethics Committee of the Cruzeiro do Sul University - Brazil Platform, São Paulo, Brazil (#37766720.9.0000.8084). Written informed consent was obtained from the patient's mother after she was informed about the study.

### Consent for publication

The consent was signed by the child's mother

### Competing interests

The authors have stated explicitly that there are no competing of interests in connection with this article.

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