COVID-19 in pediatrics: case report with many complications and a good clinical outcome

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Abstract
Coronavirus disease 2019 (COVID-19) is an acute infectious disease that caused the emergence of the new serious global pandemic. The infection in children is much less prevalent than in adults and most cases are asymptomatic or have mild symptoms. Severe cases represent less than 1% of the total, therefore information about the disease in this age group is scarce compared to data in older individuals. We exposed a case of a 16-year-old male adolescent with a previous diagnosis of myelomeningocele, hydrocephalus with peritoneal ventricle bypass (PVB), recurrent urinary tract infection, epilepsy, and obesity. The patient presented cough and convulsive crises, which worsened during hospitalization with severe acute respiratory syndrome due to SARS-CoV-2, septic shock, and cardiorespiratory arrest and invasive mechanical ventilation (IMV) for 9 days was required. Also presented several other complications and factors of critical prognosis, such as elevated inflammatory markers (C-reactive protein, D-dimer), elevated cardiac troponin, and the necessity of renal replacement therapy. Nevertheless, the clinical outcome was satisfactory and he was discharged after a 40-day stay in the Pediatric Intensive Care Unit.
INTRODUCTION

The coronavirus 2019 disease, called COVID-19, caused by Sars-CoV-2, is a potentially serious acute respiratory infection, responsible for the severity of the new pandemic declared by the World Health Organization (WHO) in January 2020, which began in China at the end of 2019\(^1\). Severe forms of the disease represent about 14% of cases\(^2\). However, the infection is less prevalent in children than in adults, usually with mild and self-limiting symptoms\(^1\).

Thus, data in infants are very scarce in relation to the literature already published on this infection in adults. Studies suggest that comorbidities may be related to the development of severe forms of COVID-19 in children\(^3,4\).

In these settings, we report the case of an adolescent with critical COVID-19 with several factors associated with severity and complications, but with good clinical outcome.

CASE DESCRIPTION

A 16-year-old male patient with myelomeningocele and hydrocephalus, with ventricular peritoneal shunt (PVD) and a history of recurrent urinary tract infections, epilepsy, and grade II obesity [Body Mass Index = 36.7]. It started with dry cough and no fever. On the same day, he was admitted to the service of origin due to seizures and was submitted to orotracheal intubation (OTI) due to a lowered level of consciousness, and was referred to the Pediatric Intensive Care Unit (PICU) of our clinic.

Upon physical examination, he had bilateral crackles on pulmonary auscultation, with no signs of hemodynamic instability. On admission, his laboratory tests showed leukopenia (3300/µL), increased rods (20%), C-reactive protein 39.8 mg/L (VR: <10 mg/L). Reverse transcription and polymerase chain reaction (RT-PCR) tests for Sars-CoV-2 were positive, his viral panel (RT-PCR) and test for Influenza - through rapid Immunochromatography came back negative - about 48 hours from the onset of symptoms. His chest radiographies showed bilateral opacities. Images 1-2 shows his Chest-CT findings Figure 1 - 2.

On the day of admission, he had an accidental extubation and was maintained with oxygen therapy in a non-re-breathing mask. We started therapy with hydroxychloroquine and azithromycin, in addition to ceftriaxone, empirically due to changes in infectious markers. Two days after admission to the PICU, the patient evolved with worsening respiratory pattern and acute respiratory distress syndrome (ARDS), requiring OTI with invasive mechanical ventilation (IMV) in high parameters, although showing adequate lung compliance.

On the fifth day of hospitalization, the patient developed urinary septic shock - due to extended-spectrum beta-lactamase-producing Klebsiella pneumoniae (ESBL), requiring the use of multiple vasoactive drugs and corticosteroid therapy for refractory shock. He had a cardiopulmonary arrest (CPA) for 4 minutes in the context of severe hemodynamic instability and myocardial ischemia, evidenced by electrocardiographic (ST-segment elevation) and laboratory markers [troponin 198 pg/mL (VR: <19 pg/mL) and CK-MB 38 U/L (VR: <16 U/L)]. The patient evolved with acute renal failure, signs of fluid overload, requiring Renal Replacement Therapy (RRT) with continuous veno-venous hemodiafiltration, followed by conventional hemodialysis. He also presented a serial increase in D-dimer of up to 15,105 µg/L (VR: <500 µg/L) and was anticoagulated with unfractionated heparin – used because of the alteration in renal function and use of RRT. He was extubated after nine days of IMV, with RT-PCR for Sars-CoV-2 negative, 30 days after admission. Afterwards, he presented PVD dysfunction, being submitted to external ventricular drainage (EVD), later...
reverted to PVD. He was discharged from the hospital after 40 days of hospitalization Table 1.

COMMENTS

We describe a severe case of COVID-19 in a 16-year-old adolescent, with the presence of several indicators related to a more severe form of the disease, but with a favorable outcome.

We know that, although children are more vulnerable to diseases, most cases of COVID-19 involving children are mild, which accounts for a much lower percentage of the disease in this population than in adults. The first retrospective study evaluating the disease in pediatric patients analyzed 2,143 cases in China, where less than 1% had severe or critical illness, and more than half had mild disease. The available epidemiology literature reports on an incidence of 3% of severe illness and 0.6% of critical illness in this age group.

Our patient initially presented mild respiratory symptoms, being hospitalized at that time for neurological symptoms (seizures). In children hospitalized with COVID-19 in the PICU in the United States (USA) and Canada, their respiratory symptoms initially were not so serious, with admission to the PICU for other reasons. In this context, a high index of suspicion for the disease in this population is important, as they are often asymptomatic, with mild symptoms or even with no respiratory signs, and have gastrointestinal signs - which may be the only clinical manifestation in pediatric patients - more common than in adults.

Data is limited in children regarding possible risk factors associated with critical illness by Sars-Cov-2. In an analysis of 345 cases, the most prevalent comorbidities were: asthma, neurological disorders, diabetes, obesity, cardiovascular disease and malignant/hematological diseases. A study carried out in New York evaluated clinical characteristics and outcomes of critical cases in children and adolescents with COVID-19 and demonstrated that the presence of comorbidities, including obesity, has been described as one of the risk factors for worsening the disease in young children. In addition, it has been suggested that a subset of pediatric patients may develop severe disease when they have significantly higher markers of inflammation: C-reactive protein, pro Atrial Natriuretic Peptide (BNP) and procalcitonin, which likely contributes to the high rate of ARDS in these patients. Severe sepsis and septic shock were also observed in 53.8% of the PICU patients, ARDS in 77% and the need to use IMV with an average of 9 days in 46.2%, the correlation of the cited markers with the exposed case is evident.

We know that COVID-19 is associated with a high inflammatory burden, which can result in cardiovascular complications - myocarditis, heart failure, arrhythmias, acute coronary syndrome, rapid deterioration and sudden death - and our patient presented severe hemodynamic instability associated with myocardial ischemia and CRP at the time. It was not evident whether acute systolic heart failure in the context of this infection is mediated by myocarditis, cytokine storm, small vessel thrombotic complications, microvascular dysfunction or a variant of stress-induced cardiomyopathy, so that the etiology of myocardial stress in this case cannot be well elucidated.

The patient in question also had greatly increased levels of D-dimer, which is associated with worse outcomes. We know that the identification of patients at high risk is important so that prophylactic measures for venous thromboembolism

| Table 1. Main laboratory test results. |
|--------------------------------------|
| **RT-PCR COVID** | **Influenza Fast Test** | **Leucocytes (µL)** | **Lymphocytes (µL)** | **C-Reactive Protein (mg/dL)** | **Troponin (µg/mL)** | **CK-MB (U/L)** | **D-dimer (ng/dl)** | **Creatinine (mg/dL)** |
| D1 | D2 | D6 | D10 | D17 | D24 | D31 | D35 | 199.8 |
| 3300 | 23300 | 10210 | 858 | 2563 | 2859 | 44.4 | 38 | 15105 |
| **Legend:** (+) = detectable; (-) = not detectable; (D) = refers to the days of hospitalization.
can be instituted, so that, in this situation, we chose to use unfractionated heparin due to kidney injury and the need for RRT.1

We can also mention the presence of other criteria for unfavorable evolution, such as seizures, altered level of consciousness and septic shock. Patients with severe disease have neurological complications, possibly resulting from viral invasion of the central nervous system, and there may be acute cerebrovascular disease, altered consciousness, seizures, neuralgia, skeletal muscle injury, meningitis and encephalitis. In a case series, septic shock was present 4% to 8% of the patients, and low-dose corticosteroid therapy is recommended for refractory shock. As for acute kidney injury, also present in this child, possible causes are hemodynamic changes, hypovolemia, renal tubular damage caused by the virus, thrombotic processes, glomerular pathology or rhabdomyolysis.2

Intubation and IMV were instituted in the face of acute deterioration (presence of fatigue and risk of exhaustion due to respiratory distress), and a protective ventilation strategy was chosen - low tidal volume and low inspiratory pressure - which was done through the use of ventilatory volume controlled with regulated pressure (PRVC).1,2 The ventilatory pattern initially described in this patient corroborates what has been reported in the literature. Soon after the onset of respiratory distress, the patient maintained good compliance, despite severe hypoxemia in the progression of the disease, with a need for higher positive end-expiratory pressure (PEEP) to maintain adequate oxygenation, a condition compatible initially with the stage of the disease called L-type, and then, consistent with the H-type — clinical scenario of typical ARDS.3

Finally, the patient had a viral load for a long period, which can be expected in critically ill patients. In this context of severity and based on the above, we can mention the factors associated with worse clinical evolution and increased risk of death: male gender, presence of comorbidities, dyspnea, leukopenia, renal impairment, elevation of inflammatory markers, increase in cardiac troponin, D-dimer elevation, sepsis.4

Literature on the clinical picture of severe COVID-19 in children is scarce, especially in Brazil. Thus, we hope that this report and discussion of this case will contribute - as a form of evidence - to the knowledge available about this pathology in Pediatrics, considering that it is an emerging disease, with a pandemic character, which greater understanding makes it possible to optimize the management of these patients by healthcare professionals.

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