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CASE REPORT

Complete recovery post severe-covid-19 in a patient with type 2 mucopolysaccharidosis

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Abstract

Introduction: Children with comorbidities are at greater risk of developing severe forms of Covid-19. This paper reports a case of Mucopolysaccharidosis Type 2 (MPS-II) that presented complete recovery after severe Covid-19. **Case description:** Male, 13 years old, with MPS-II, is seen in a pediatric emergency room due to respiratory distress, airway hypersecretivity and fever. On physical examination, he had room air desaturation, snoring and diffuse coarse rales on pulmonary auscultation. Laboratory tests revealed: rod-like cell count, cytoplasmic vacuolization in neutrophils, thrombocytopenia, consumption coagulopathy, toxic level of valproic acid, respiratory acidosis and metabolic alkalosis; in addition to positivity for Covid-19. Chest radiography showed perihilar infiltrate with retrocardiac consolidation. Computed tomography of the chest showed bilateral perihilar and basal consolidations, in addition to bilateral endobronchial dissemination. Electrocardiogram showed changes in ventricular repolarization and ST-segment depression. Thus, Covid-19 infection was diagnosed, with secondary bacterial pneumonia and hemodynamic and cardiac repercussions, concomitant valproic acid intoxication. The patient required intensive care for 22 days, mechanical ventilation support for 19 days, in addition to the use of vasoactive drugs. He was discharged from hospital after 49 days, with gastrostomy, tracheostomy and home oxygen. **Comments:** MPS-II carriers tend to have most severe form and worse prognosis when infected with Covid-19. This is because there are factors inherent to MPS-II that make it difficult to recover after pulmonary infections, such as: previous pulmonary dysfunction, macroglossia, adenoid hypertrophy, hypersecretivity and hypotonia. Such factors reflect the long hospital stay of patient reported when they get Covid-19.

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INTRODUCTION

Mucopolysaccharidoses (MPS) correspond to an inborn error of metabolism characterized by a deficiency of lysosomal enzymes. Such a deficiency leads to the buildup of glycosaminoglycans (GAG), with each variant corresponding to the deficiency of a specific lysosomal enzyme[1].

Mucopolysaccharidosis type 2 (MPS-II), also called Hunter syndrome, has an estimated occurrence in Brazil of 0.37:100,000 live births[2]. The disease results from the deficiency of iduronate-2-sulfatase, which is responsible for the degradation of dermatan sulfate and heparan sulfate GAGs[3].

MPS-II can cause manifestations such as: facial anomalies, seizures, hepatosplenomegaly, airway compromise, macroglossia, hypersecretion, laryngomalacia and tracheobronchomalacia[4]. Therefore, patients with Hunter syndrome tend to have more severe conditions and an unfavorable evolution when they contract pulmonary infections, such as Covid-19[5]. In addition, children with comorbidities are at greater risk of the severe form of Covid-19 infection and, consequently, higher mortality[6].

Therefore, we report the case of an MPS-II patient who, with adequate support and management, presented adequate recovery after contracting a severe infection by Covid-19.

CASE REPORT

Male, 13 years old, epileptic (under valproic acid, 46.8 mg/Kg/day), hydrocephalic (with ventriculoperitoneal shunt) and with Mucopolysaccharidosis Type 2 (MPS-II) (under Replacement Therapy Enzyme (RTE) since his diagnosis at 5 years of age). He is treated at the emergency room due to a worsening of his breathing pattern for the past 3 days, associated with changes in airway secretion (greater quantity, thicker and greenish), and two febrile episodes in the last 24 hours. The patient had close contact with a family member infected with Covid-19.

Upon physical examination, he was not communicative, with global muscle hypotrophy, joint stiffness, broad nose, macroglossia, in addition to dental abnormalities - characteristics reported as baseline for the patient (Figure 1). On pulmonary auscultation, he presented bilateral vesicular murmur, with snoring and diffuse thick rales, showing unsaturation in ambient air. Chest X-ray showed perihilar infiltrate with retrocardiac consolidation. Laboratory tests revealed: increased rod counts (27% = 1,695/mm3), cytoplasmic vacuolization in neutrophils, thrombocytopenia (48,000/mm3) and increased international normalization ratio (INR) (1.47). Viral screening was positive for Covid-19.

Ventilatory support was started with oxygen in a non-breathing mask, corticosteroid therapy and antibiotic therapy with ampicillin-sulbactam - due to the diagnostic hypothesis of pneumonia secondary to micro aspirations, since he already had difficulty in swallowing (as expected in the evolution of the underlying disease).

On the second day of hospitalization, he presented worsening of respiratory effort, tachypnea and unsaturation. Chest computed tomography showed bilateral perihilar and basal consolidations, in addition to signs of bilateral endobronchial dissemination (Figure 2). The clinical picture and complementary tests were compatible with bacterial pneumonia secondary to Covid-19.

On the same day, he had profuse epistaxis, requiring nasal packing with adrenaline to stop the bleeding. He was seen by an otorhinolaryngologist and an hematologist, opting for the use of nasal saline solution and intravenous epsilon-aminocaproic acid.

The hypothesis of thrombocytopenia associated with the use of valproic acid was raised, so the patient's anticonvulsant agent was changed. Subsequently, serum levels of valproic acid corroborated this hypothesis, showing a toxic level (above 150 ug/mL) at that time.

On the fourth day of hospitalization, the patient's breathing pattern worsened, with significant subcostal and furcula retraction, and saturation between 87-89% using a non-rebreathing mask at 12L/min. Inhaled salbutamol and intravenous magnesium sulfate were performed, in addition to respiratory physical therapy, but the patient did not show clinical improvement and was transferred to the Intensive Care Unit (ICU).

Arterial blood gas analysis upon admission to the ICU showed respiratory acidosis and metabolic alkalosis. We chose to use continuous positive airway pressure (CPAP), in addition to intensifying respiratory physical therapy and prone positioning. However, the patient was extremely agitated and uncomfortable, requiring support with mechanical ventilation (MV). Due to the difficulty in managing the upper airway in patients with MPS-II, with macroglossia and limited mouth opening, it was necessary to perform an emergency tracheostomy, and maintain high ventilatory parameters on MV.

The patient used magnesium sulfate and methylprednisolone to manage the pulmonary condition. Sedation and analgesia with fentanyl, midazolam, methadone and ketamine were maintained. He was administered curare due to asynchrony with the ventilator. He required noradrenaline as a vasopressor drug due to hypotension to maintain hemodynamic stability. In addition to needing albumin replacement and electrolyte correction. As for antibiotic therapy, the spectrum was expanded, starting ceftriaxone and clindamycin. Furthermore, he used enoxaparin to avoid thromboembolic complications.

There was an alteration on the electrocardiogram in the ventricular repolarization and ST-segment depression, which was later normalized.

There was a gradual recovery of the respiratory failure condition, with gradual weaning from mechanical ventilation, with definitive uncoupling on the 19th day of MV use. After 22 days in the Pediatric ICU, the patient was transferred to the ward, with blood gas tests within normal limits.

In agreement with the multidisciplinary team, there was a need for gastrostomy for the patient's nutrition, due



Figure 1. Patient's facies (Authorized by the mother).

to his impossibility to feed properly orally, as expected due to the progression of the underlying disease. The procedure was performed on the 41st day of hospitalization, and after the diet was progressed via gastrostomy, according to the protocol of the clinic.

The patient was discharged after 49 days of hospitalization, in good general condition, with tracheostomy, gastrostomy and low flow oxygen to use at home (0.5-1 L/min); remaining in outpatient follow-up with medical specialties.

DISCUSSION

Hunter's syndrome has heterogeneous clinical manifestations, since it affects the most varied organs and systems[7], among them, the reported patient had: characteristic facial anomalies such as a broad nose, macroglossia, dental abnormalities; hydrocephalus, convulsions; and joint stiffness[3,4,8]. These characteristics usually appear between two and four years of age, being absent at birth; yet, the patient may present normal initial neuropsychomotor development, which makes the early diagnosis of the disease difficult[9]. In the reported case, the diagnosis was made only at five years of age.

Respiratory system involvement is frequent in this pathology, which occurs due to the deposition of glycosaminoglycans in the airways, causing progressive dysfunction of lung function, the restrictive type being more common. In the upper respiratory tract, macroglossia and adenoid hypertrophy together with an increase in mucus secretion predisposes to

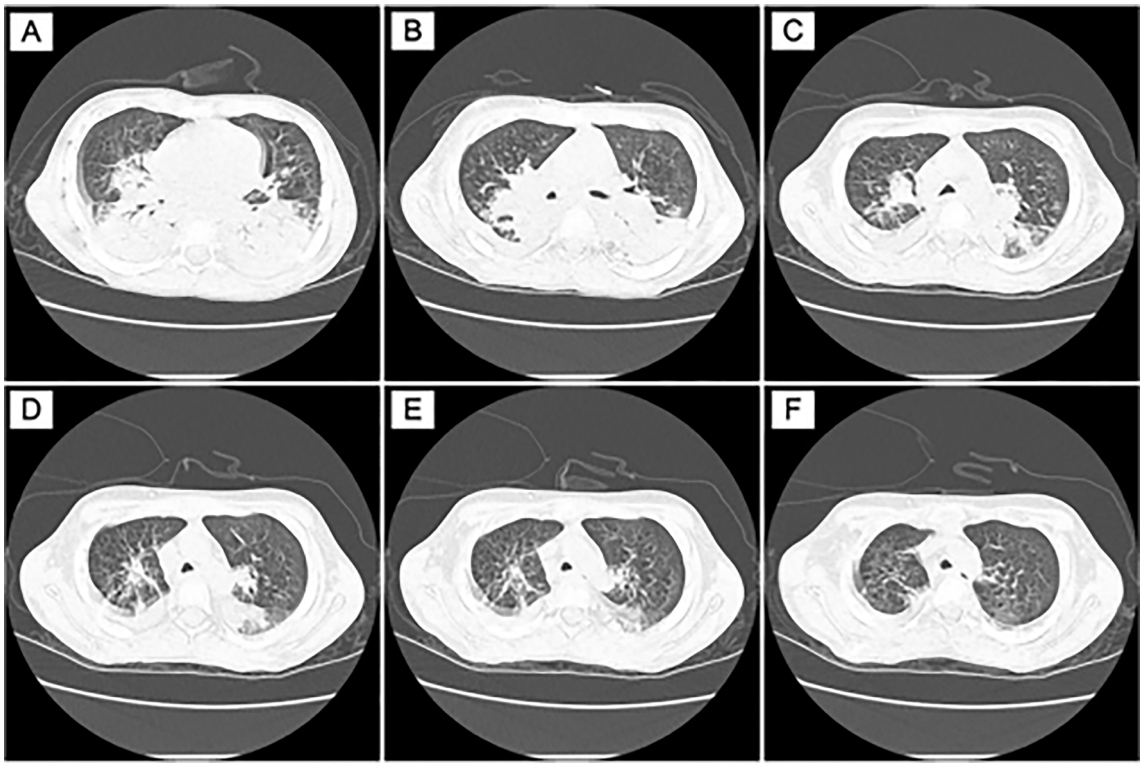


Figure 2. Computed tomography of the chest demonstrating bilateral peribronchovascular pulmonary opacities, with pulmonary consolidations with air bronchograms and a slight atelectatic component in the lower lobes. Thickening of the bronchial walls of the lungs and extensive centrilobular micronodules with bilateral "tree-in-bud" images, notably in the right upper lobe. Small pleural effusion on the right and minimal laminar effusion on the left.

airway obstruction. Such repercussions made orotracheal intubation difficult in the case described, and tracheostomy was necessary to obtain a definitive airway in this patient.

Enzyme Replacement Therapy (ERT) tends to improve lung function and thereby bring quality of life to these patients[11]. When instituted early, before 1.5 years of age, it brings about even better results, reducing morbidity[12] and mortality by up to 54%[10]. In the reported patient, ERT was started late, after his diagnosis at 5 years of age.

In general, children have lower rates of Covid-19 infection and have fewer clinical repercussions when compared to adults. However, among children who become infected, those with comorbidities tend to have a more severe condition and worse prognosis. Children with heart disease, diabetes and/or non-asthmatic chronic lung diseases are the most affected by Covid-19. The infection favors the deterioration of the underlying disease, with pulmonary function being the most compromised[13].

The study by Pierzynowska et al indicates that MPS patients are less likely to develop Covid-19 infection. This is justified by transcriptomic analyzes of genes involved in viral development, and patients with MPS have 4 of these genes in "down-regulation" and only 2 of them in "up-regulation"[7].

On the other hand, it is known that MPS-II involves changes in the airway, such as thick secretion and hypotonia, which naturally determines a predisposition to contract lung diseases and/or be more severe when contracting Covid-19. What corroborates this statement was the fact that the patient described required a longer hospital stay and more intensive care than the pediatric average[5,13].

The length of stay in the ICU of the reported patient was 22 days, a much higher number than that described in the literature for the pediatric population, which is approximately 5 days[14]. The patient's main approach was respiratory support, requiring 19 days on Mechanical Ventilation (MV). Although most pediatric patients require oxygen therapy, less than half are on MV and the median number of days of use is 7.7[14].

Regarding the medications, as pointed out in the literature, the patient received antibiotic therapy according to the management of the Severe Acute Respiratory Syndrome[14]. In addition, anticoagulants were used, which although there is uncertainty of direct benefit for the treatment of Covid-19, there are benefits when used in critically ill and bedridden patients, such as antithrombotic prophylaxis[15], which includes the condition of the reported patient. In this case no experimental antiviral therapies were used.

The importance of multidisciplinary follow-up and adequate treatment in children with MPS-II is highlighted. Such actions, added to an early diagnosis and proper management of possible infections, such as Covid-19, are essential for a good clinical evolution in unfavorable situations.

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