Successful ECMO therapy in a child with COVID-19-associated ARDS and Ewing's Sarcoma.

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Abstract

Most children and adolescents with SARS-CoV-2 infection shows asymptomatically or with mild symptoms. There are few reported cases of extracorporeal membrane oxygenation (ECMO) in pediatric patients with coronavirus disease 2019 (COVID-19). We present a previously healthy 13-year-old male, diagnosed with metastatic Ewing's sarcoma at the same time as catastrophic acute respiratory distress syndrome due to COVID-19, which was successfully supported by veno-venous ECMO, while he received the corresponding chemotherapy protocol. ECMO can be used as salvage therapy in oncology pediatric patients with respiratory failure secondary to COVID-19. In addition, successful chemotherapy can be administered while patients are supported on ECMO.

INTRODUCTION

SARS-CoV-2 mainly affects adults, many of whom require Intensive Care Unit (ICU) admission and present significant morbidity and mortality[1]. Most children and adolescents present the infection with mild or without symptoms, but those with medical histories can be susceptible to more severe forms of disease[2]. There are few reported cases of extracorporeal membrane oxygenation (ECMO) management in pediatric patients with coronavirus 2019 disease (COVID-19)[3–8]. We present the case of a previously healthy 13-year-old male, diagnosed with metastatic Ewing's sarcoma at the same time as developing catastrophic acute respiratory distress syndrome (ARDS) due to COVID-19. He was successfully supported by prolonged veno venous-ECMO (VV-ECMO), while starting chemotherapy.

CASE REPORT

We present a previously healthy thirteen-year-old male. Parents and siblings were diagnosed with COVID-19. On 04/14/21, he consulted, and was admitted to his hospital of origin with progressive respiratory distress. Chest computed tomography (CT) (Figure 1A) showed massive left pleural effusion and multiple nodular lesions in the right lung. In this context, he was connected to non-invasive mechanical ventilation, empiric antibiotic therapy was started, evacuating thoracocentesis was performed, and a pleural catheter (PC) was placed. Blood tests showed elevated inflammatory markers (C-reactive protein (CRP) 191 mg/L, ferritin 535 ng/ml). In addition, tomographic abdominal and pelvic exploration (Figure 1B) showed a multilobed, heterogeneous pelvic mass. Brain CT was normal. SARS-COV-2 was confirmed by polymerase chain reaction, so dexamethasone was initiated. The patient evolved towards severe respiratory distress and hypoxemia, was connected to invasive mechanical ventilation (IMV), and transferred to the Pediatric Intensive Care Unit (PICU) of the corresponding reference hospital.

Upon transfer, he was described as feverish, pale, tachycardic and hypotensive, requiring norepinephrine, that could be suspended four days later. He presented torpid respiratory evolution with severe ARDS, requiring prone position ventilation and neuromuscular blockade. Discrete initial improvement was observed, but

on day 11 of hospital admission (04/25/21), he deteriorated, presenting right pneumothorax, another PC was installed. A new chest CT was performed that ruled out pulmonary thromboembolism. Despite these measures he continued hypoxemic (PaO_2/FiO_2 50, oxygenation index 29) and lung protective ventilation was impossible to sustain. VV-ECMO was decided.

Etiologic study for the pelvic mass was performed including: beta-human chorionic gonadotropin and alpha-fetoprotein (normal), pleural fluid flow cytometry for malignant hematological diseases (negative) and an ultrasound-guided biopsy of the pelvic mass was made 9 days after hospital admission, which confirmed Ewing's sarcoma. Protocol chemotherapy was initiated (on day 16 of admission), with our patient already on VV-ECMO.

He continued in critical condition, with suitable perfusion parameters, but without improvement of ARDS. Acute kidney injury developed which, added to fluid overload, required continuous renal replacement therapy through the ECMO circuit for 15 days. He continued with high inflammatory biomarkers (maximum CRP 343 mg/dl); antimicrobial coverage was changed empirically to vancomycin, meropenem, voriconazole and cotrimoxazole. Bronchoalveolar lavage (BAL) was performed and ruled out bacterial, fungal, or viral intercurrence. Due to torpid evolution, compatible with acute fibrinous organizing pneumonia, steroid dosage was increased, changing dexamethasone for methylprednisolone (10 mg/kg daily for 3 days), and maintained subsequently with prednisone in progressively decreasing doses. After that, a decrease in inflammatory parameters was observed but without improvement in respiratory state.

During the third week from admission, he presented new significant respiratory compromise, secondary to ventilator-associated pneumonia due to *Candida parapsilosis* isolated in a second BAL culture, specific treatment with caspofungin was started. In addition, left pleural effusion increased and right pneumothorax reappeared. This required the installation of a new right PC, and in attempt to improve oxygenation, prone position on ECMO was used for 6 days (from day 22 of admission, 11 on ECMO). For management of the left pleural effusion, fibrinolytic therapy was administered (recombinant tissue plasminogen activator (rt-PA)). A new chest CT scan was performed (Figure 2) that showed bilateral pleural effusion, greater in the right lung, with large organized collections of blood content that produce a mass effect on adjacent pulmonary segments. Due to the patient's condition, resolution of the pulmonary clot was attempted with pleural administration of rt-PA. He presented partial response, but also bleeding. Therefore, at 44 days from admission and 34 of ECMO, he was taken to the operating room for video-assisted thoracoscopic surgery, where a collection of clots was identified and cleaned at the level of the thoracic cavity, an inflamed-looking lung, especially in the middle lobe, which appeared to be an intraparenchymal hematoma. After the procedure, respiratory improvement was finally observed, but given prolonged IMV, tracheostomy was performed in the PICU, 30 days after admission. He presented progressive improvement, weaning from ECMO was possible, and decannulation was performed after 42 days of VV-ECMO support. Maintained improvement led to IMV weaning after 85 days of hospital admission.

There were no other hematological complications, and they did not present neurological complications, except myopathy of the critical patient.

Our patient continued his treatment with chemotherapy according to protocol. In addition, a rehabilitation program was carried out in the PICU, being able to decannulate tracheostomy on day 118. He was moved to Oncology 2 days later and finally discharged from hospital after 138 days with a Karnofsky score of 70. He is currently undergoing his outpatient controls in Oncology.

DISCUSSION

There are several reports of ECMO use in adult patients with coronavirus COVID-19 who develop ARDS[9]. Ramanathan et al. reported that the majority of patients received VV-ECMO support and that the mortality in these patients was 37.1%, similar to those with non-COVID-19-related ARDS.

Nevertheless, there are no systematic reviews or case series with a high number of pediatric patients who have required ECMO therapy. The European Chapter of the Extracorporeal Life Support Organization

(ELSO) reported a case series of only 7 children that required ECMO from reports from 52 centers[3]. The majority required veno-arterial ECMO and only in 3 cases the indication for ECMO was hypoxemia. The mortality in this case series was 43%. Apart from this series, there are a few publications of isolated case reports of COVID-19 and ECMO in pediatric patients[4-8]. In them, the patients described are mainly adolescents, some with previous comorbidities. All the patients described in these case reports reviewed survived except one; however, thrombotic events were frequently reported despite use of anticoagulation protocols. While these events are common on ECMO, COVID-19 has been associated with the increase in the risk of thrombosis. For this reason, the ELSO guidelines recommend a close monitoring of coagulation, ideally based on thromboelastography[10]. Effectively, in the case of our patient, his main complication was a hemothorax, probably due to coagulation disorders aggravated by chemotherapy treatment.

Another important aspect of our patient and about which there is also little reported experience, is the use of chemotherapy during ECMO support. In the bibliographic review carried out, we only found a case report of a pediatric patient with a T-cell lymphoblastic lymphoma who received chemotherapy during ECMO support[11]. In that patient and in ours, we showed that successful chemotherapy can be administered while the patient is on ECMO support, despite underlying and nosocomial infections.

CONCLUSION

ECMO can be used as salvage therapy in pediatric patients with respiratory failure secondary to COVID-19, including patients with important comorbidities. This case also illustrates that oncology patients can be supported on ECMO by multidisciplinary teams and that therapeutic chemotherapy protocols can be employed.

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Nothing to declare.

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FIGURES

Figure 1A. Initial chest computed tomography

Figure 1B. Initial abdomen-pelvis computed tomography

Figure 2. Chest computed tomography showing hemothorax.