

CASE REPORT

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ECMO complications in COVID-19: A new insight of a controversial disease

Beatriz Amorim Beltrão, Rafael Cabral Teixeira, Diego Bastos Porto

ABSTRACT

Introduction: Extracorporeal membrane oxygenation (ECMO) is a support therapy that can be used in patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and refractory hypoxemia, despite optimal management. However, ECMO may be responsible for a synergic effect in the proposed mechanism of viral associated hyperinflammation.

Case Report: We report a rare case of hemophagocytic lymphohistiocytosis (HLH) in a 58-year-old obese man, who initially responded well to ECMO support and ICU care. He later progressed to a clinical scenario that met criteria for the diagnosis of HLH. Despite our best efforts, the patient had a fatal outcome. To the best of our knowledge, this is the first report of such association.

Conclusion: This case highlights the importance of the appropriate timing in the diagnosis and treatment of SARS-CoV-2 infection and complications, mainly those that are rare and poorly understood, as HLH in patients with ECMO support. The outcomes may be improved with earlier recognition of these grim scenarios.

Keywords: Case report, COVID-19, Extracorporeal membrane oxygenation, Hemophagocytic lymphohistiocytosis

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INTRODUCTION

SARS-CoV-2 pandemics bought many uncertainties to the healthcare professionals' community. Current knowledge suggests that the cornerstone of therapy in critically ill patients is based on organ dysfunction support associated with corticosteroids [1]. Among the potentially useful support strategies is extracorporeal membrane oxygenation (ECMO). Recently, however, the Extracorporeal Life Support Organization published data with an astonishing 39% mortality rate and high complication incidence associated with this modality [2]. Also, mortality predictions scores were validated such as ISARIC-4C (International Severe Acute Respiratory and Emerging Infections Consortium Coronavirus Clinical Characterisation Consortium) [3]. Aiming to aid in disease comprehension and add new insights to its perspective of complications, we describe a fatal case of a patient with SARS-CoV-2 infection, on ECMO, complicated by the rare diagnosis of hemophagocytic lymphohistiocytosis (HLH), which might have had a different outcome if the diagnosis had been suspected earlier. We highlight the hypothesis of a synergic association between SARS-CoV-2 infection and ECMO, which may contribute to a higher HLH incidence. We also stressed its contribution to deleterious patients' outcomes, if not suspected early in the evolution.

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CASE REPORT

We report a case of a 58-year-old male, with hypertension and obesity (BMI=31 kg/m²), who was admitted to the hospital with a six-day history of daily fever, headache, and dry cough. He also complained of moderate dyspnea, which began 24 hours prior to seeking medical assistance. At the emergency department, he had a breath rate of 25 and an O₂ saturation of 86% on room air. He was started on 6 L/min oxygen, corticosteroids, and a reverse transcription-polymerase chain reaction (RT-PCR) nasal and oropharynx specimen was collected, together with other laboratory exams and a chest-computed tomography (CT) (Table 1, Figure 1). His ISARIC-4C risk score was 12/21, which predicted a mortality rate of 32.9%, at hospital admission. Due to worsening of symptoms and hypoxemia, a decision to intubate was made and he was transferred to the ICU.

On admission, he was started on protective lung ventilation strategy with 5 mL/kg tidal volume and a target *driving pressure* of 15 or lower. At this point, he was on 100% FiO₂ and arterial blood gas analysis showed a PaO₂ of 70 mmHg. A decision to initiate prone positioning was then made, together with a consultation with the ECMO team. Due to a persistent PaO₂/FiO₂ under 60 and a PCO₂ >80 mmHg, despite optimal therapy, a decision to initiate venovenous-ECMO was made.

Our patient initially responded well to ECMO and ultraprotective ventilation strategies, despite having a high predicted mortality rate. He even began to wean sedation and ECMO. However, since the beginning of follow-up, he showed high ferritin and triglycerides levels, had an enlarged spleen, and, on the course of disease, developed a progressive decrease in hemoglobin and platelets (Table 1). Also, around his eleventh follow-up day, he required a new increase in ECMO support. After excluding other etiologies, such as new onset infection and bleeding, based on the clinical picture and evolution, a hypothesis of hyperinflammation and possible HLH was made. After a consultation with hematology, a decision

to infuse Etoposide was made as a last resort to revert the potentially fatal evolution. About 72 hours later, the patient was hemodynamically unstable, had multiple bleeding sites and remained without an evident infection site, despite being continuously hyperthermic. He died shortly afterwards.

DISCUSSION

The development of immune complications wasn't at all anticipated and constituted an exceptional and complex case. Hemophagocytic lymphohistiocytosis is a potential hypothesis to describe some complications of SARS-CoV-2 infection [4]. Its diagnosis is based on clinical and molecular criteria previously described [5] and reinforced by the H-Score [4] prediction. Genetic and functional testing are not recommended for routine use because such abnormalities are rarely detected [5]. Our patient had an initial H-score predicting a 98–99% chance of a diagnosis and fulfilled criteria based on expert consensus [5]. Although the relation among secondary HLH (sHLH) and cytokine release syndrome has been previously discussed in COVID-19 patients, we add the perspective of the possible higher incidence of sHLH in COVID-19 patients due to the influence of ECMO. Thus, ECMO, which by itself can promote sHLH, due to its underlying pathophysiology implications, as other extracorporeal therapies, might have played a key role in this complication [6]. This may be due to a synergic mechanism with the hyperinflammation secondary to viral infection, emphasizing the importance of a high level of suspicion for an early diagnosis and prompt therapy. This scenario may be suspected in patients with high levels of cytokines, ferritin, triglycerides, and other markers as highlighted previously [4, 5]. The potential therapeutic options focus on controlling the inflammatory cytokine production and includes drugs like etoposide [5]. The infusion should occur early in the disease course in order for it to better optimize treatment. This occurs

Table 1: Laboratory tests according to follow-up days

Laboratory tests	Follow-up days								
	Day 1	Day 3	Day 4 [§]	Day 6	Day 8	Day 12	Day 15	Day 17	Day 18 [†]
Hemoglobin (g/dL)	14.2	13.5	13.2	11.3	9.2	7.8	8.6	7.4	7.0
WBC (*10 ⁹ /L)	8.7	10.8	16	50.5	60.7	70	28.4	29.7	35.3
Neutrophils (*10 ⁹ /L)	7.13	7.66	13.44	43.43	37.34	66.50	23.85	25.54	33.53
Platelets (*10 ⁹ /L)	148	235	278	344	393	265	98	56	67
Ferritin (ng/mL)	3000	3500	–	6500	4300	1291	1301	3000	–
Triglyceride (mg/dL)	–	–	–	486	451	299	107	145	–
Fibrinogen (mg/dL)	998	1200	–	778	876	576	849	–	–
AST (IU/L)	92	83	127	255	172	106	104	276	196
CRP (mg/dL)	23.4	24.7	14.5	14.7	10.5	4.2	14.6	17.8	17.6

Abbreviations: AST: aspartate aminotransferase; CRP: c-reactive protein; WBC: white blood cells.

[§]ECMO cannulation day; [†]Death.

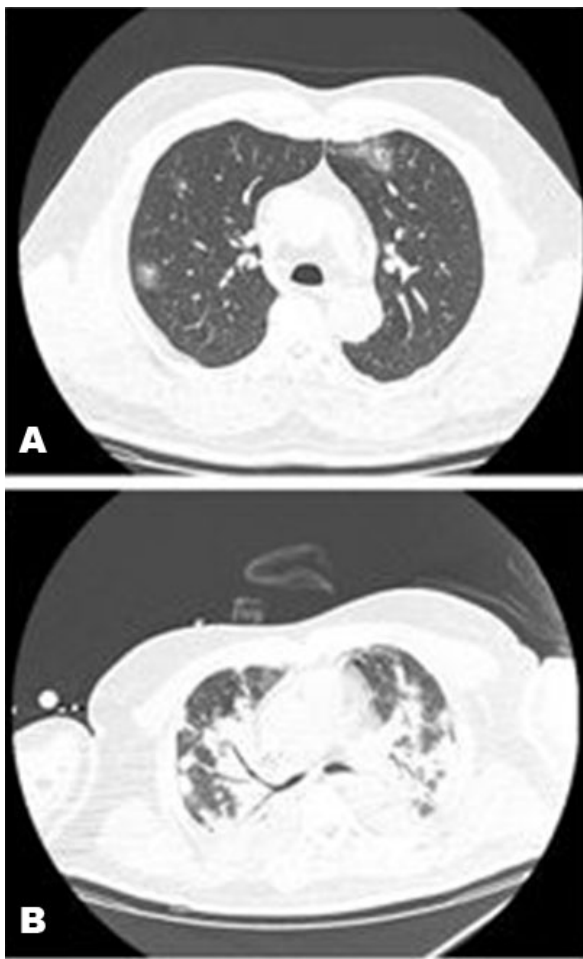


Figure 1: (A) Chest CT on day 1 of hospital admission showing multiple pulmonary ground-glass opacities, sometimes associated with interlobular septal thickening, some with confluent areas of consolidation, in a multifocal, bilateral, predominantly peripheral and posterior distribution. Pulmonary compromise of about 25%. (B) Chest CT on day 14 after hospital admission showing similar involvement as the previous CT, with an increase in pulmonary involvement. Now, accounting for about 75% of parenchyma.

by minimizing cellular destruction, even though its pharmacodynamics on ECMO are not well established. In this setting, it might even improve outcomes. This remains to be proven in further studies. In spite of that, we stress that, although each isolated scenario (COVID-19 or ECMO) may contribute to sHLH, the exposition to both conditions, simultaneously, as presented in this case report, creates a sHLH setting more prone to happen. This hypothesis also needs to be validated.

CONCLUSION

The potential synergic effect between SARS-CoV-2 infection and ECMO may play a role in a higher sHLH

incidence. This setting may produce an even more challenging clinical scenario. Its prompt recognition and treatment may improve clinical outcomes.

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Author Contributions

Beatriz Amorim Beltrão – Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Rafael Cabral Teixeira – Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Diego Bastos Porto – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Guarantor of Submission

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Consent Statement

Written informed consent was obtained from the patient for publication of this article.

Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

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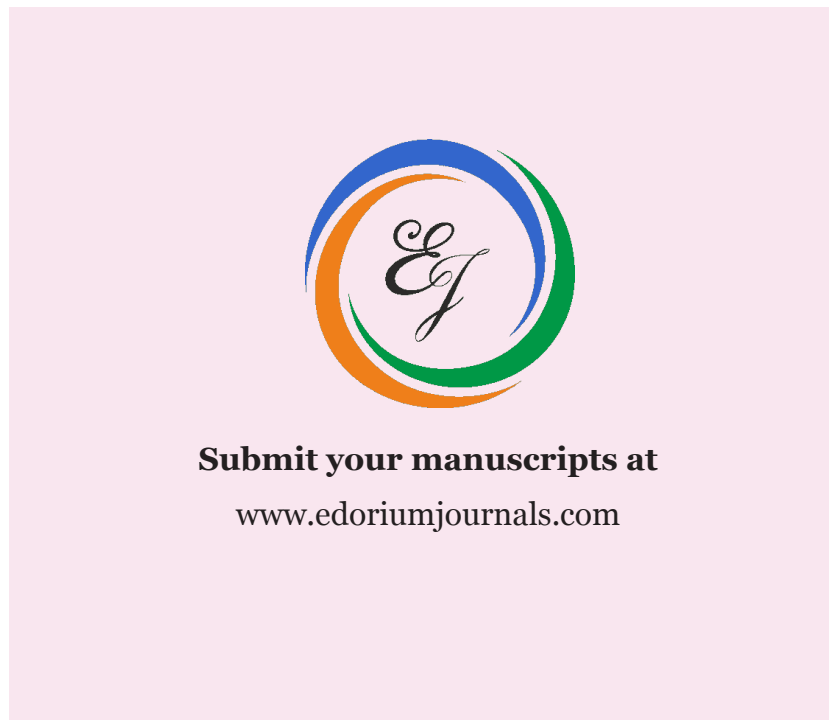
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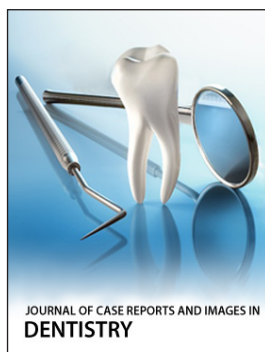
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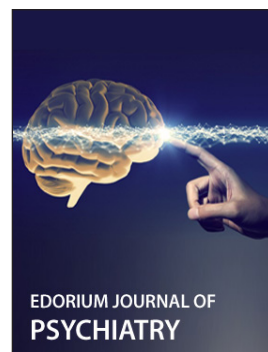
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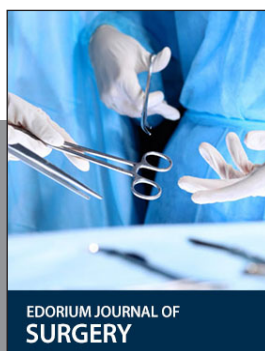
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