CASE REPORT

Multidisciplinary approach to a septic COVID-19 patient undergoing veno-venous extracorporeal membrane oxygenation and receiving thoracic surgery

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1 | INTRODUCTION

Pneumothorax is a complication in COVID-19 patients, increasing mortality by 14%. We report a male affected by severe COVID-19, complicated by hemopneumothorax, requiring extracorporeal membrane oxygenation (ECMO)

and surgery, and by septic shock. A multidisciplinary approach resulted in a good patient outcome, despite the severity of clinical conditions.

In 2020, the rapid spread of a novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection caused the epidemic of a new disease (COVID-19) mainly

Bruni and Garofalo are equally contributed for this article. UMG COVID-19 Group members are listed in Acknowledgements section.

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Abstract

A multidisciplinary approach appears to be fundamental for the treatment of critically ill patients with COVID-19, improving clinical outcomes, even in the most severe cases. Such severe cases are advisable to be collegially discussed between intensivists, surgeons, infectious disease, and other physicians potentially involved.

KEYWORDS

antibiotic therapy, COVID-19, ECMO, SARS-CoV-2, thoracic surgery

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characterized by flu-like symptoms and acute respiratory failure. The disease may complicate with severe hypoxemia, thromboembolic complications, acute respiratory distress syndrome (ARDS), and multiorgan failure secondarily to a systemic inflammatory response. Up to 15% of patients require intensive care unit (ICU) admission for noninvasive or invasive mechanical ventilation, in association with prone position and, whenever possible and indicated, ECMO.¹⁻³

Nowadays, no specific treatments for COVID-19 are available, and supportive cares, including oxygen therapy, ventilatory support, fluid management, and antibiotic treatment for secondary bacterial infections, are recommended.⁴ Furthermore, in severe and critical COVID-19 patients, pharmacologic venous thromboembolism (VTE) prophylaxis is strongly recommended, whereas therapeutic anticoagulation is only in case of VTE.⁴

We here report the case of a critical COVID-19 patient, complicated by hemopneumothorax requiring veno-venous extracorporeal membrane oxygenation (vv-ECMO) and thoracic surgery, who has been successfully treated with multiple interventions guided by a typical multidisciplinary approach.

2 | CASE REPORT

In January 2021, a 47-year-old Caucasian man (weight 80 kg; height 178 cm) was admitted to the acceptance and emergency department of a tertiary level hospital in our region for acute respiratory failure. The patient reported fever and sore throat in the past 10 days. He tested positive for SARS-CoV-2 by nasopharyngeal swab. At the hospital admission, the patient was affected by impairment of gas exchange requiring helmet continuous positive airway pressure at 10 cmH₂O, in association with prone position.³ The day after, gas exchange further deteriorated due to bilateral pneumothorax. Invasive mechanical ventilation was instituted and bilateral chest drainage was positioned. The patient was therefore immediately transferred to our hospital, referral center for ECMO in the region, for possible indication to vv-ECMO.⁴

2.1 | Intensive care unit cares

At arrival (Day 0), the patient was sedated with propofol (3 mg*kg/h), remifentanil (0.15 mcg*kg/min), and cisatracurium (0.1 mg*kg/h). Volume-controlled ventilation was instituted with a protective tidal volume (6 ml/kg of predicted body weight), a respiratory rate of 26 breaths/ min, positive end-expiratory pressure at 12 cmH₂O, and an inspired oxygen fraction (FiO₂) of one.⁴ The patient was also hemodynamically unstable, with persistent hypotension (ie mean arterial pressure <65 mmHg) despite fluid resuscitation. Continuous infusions of norepinephrine (1.4 mcg/kg/min) and glypressin (3 mcg/kg/h) were started.⁴

Urinary output was supported by continuous infusion of furosemide at 4 ml/h.

The left chest tube was oscillating and intermittently bubbling in the water-seal chamber, whereas the right one was also producing around 300 ml of blood daily. Blood test showed anemia (hemoglobin 7.2 mg/dl), a moderate increase of cardiac and muscular enzyme and augmented inflammatory indexes (C-reactive protein: 114 mg/L [normal range 0-5.0 mg/L]; procalcitonin: 1.89 ng/ml [normal range 0.5 ng/ml low risk for sepsis; >2.0 ng/ml high risk for sepsis]). At the arterial blood gases, oxygenation was severely deteriorated, as indicated by an arterial partial pressure (PaO_2) to FiO₂ (PaO_2/FiO_2) equal to 46 mmHg and an oxygenation index equal to 52. The Simplified Acute Physiology Score (SAPS) II was 63 (predicted inhospital mortality at 74%) and Sequential Organ Failure Assessment (SOFA) score was 15. No electrocardiogram alterations were found. Chest CT scan at arrival is shown in Figure 1 (panel A).

Despite optimization of the ventilation, vv-ECMO was run as rescue therapy because of refractory hypoxemia.⁴ Anticoagulation was guaranteed by continuous infusion of heparin targeted to an activated partial thromboplastin time around 60 sec. Tidal volume was reduced to 2.5 ml*kg of predicted body weight, whereas respiratory rate to 8 breaths/min. During Day 1, a continuous blood loss (around 100 ml/h) from right chest tube was observed in course of vv-ECMO.

After a collegial meeting with thoracic surgeons, a conservative management was initially attempted by optimizing the coagulative pathways (ie administration of coagulation factors, protein C, and protein S) and titrating heparin infusion, guided by both the thromboelastography (TEG) and the conventional blood coagulation tests. Despite an initial improvement, bleeding was not completely controlled and the thoracic surgeon decided to proceed with right thoracoscopy on Day 9. A second look was also done on Day 14 (see below). Noteworthy, 21 blood units were transfused.

Bleeding was then controlled and pulmonary function also improved. On Day 16, the patient was successfully weaned from vv-ECMO and at Day 17 tracheostomized. On Day 22, chest tubes were removed. Chest CT scan at Day 22 is shown in Figure 1 (panel B).

The clinical course was complicated by hospitalacquired infections (see below), which prolonged the ICU length of stay. The weaning from the ventilator occurs through pressure-assisted modality (Day 28) and,

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FIGURE 1 Figure shows the CT scan at patient's arrival (panel A), after thoracic surgeries and ECMO weaning.(panel B), and at ICU discharge (panel C)

thereafter, through heated and humidified high-flow oxygen therapy (Day 34). The patient was discharged from ICU on Day 41. Chest CT scan before ICU discharge is shown in Figure 1 (panel C).

2.2 | Surgical treatment

Given the unsuccessful attempt of the conservative treatment, on Day 9 a multidisciplinary agreement between intensivists and thoracic surgeons decided for a surgical approach and a right thoracoscopy was performed with the patient on vv-ECMO. The anesthesiologist placed a double-lumen endotracheal tube (Robertshaw 37 F), to allow a one-lung (left) ventilation. Active sources of bleeding or pulmonary air leaks were endoscopically excluded. A diffuse scattered parietal pleural bleeding was controlled by electrocautery and hemostatic material. Two chest tubes were positioned in standard fashion to monitor the possible occurrence of rebleeding. A subatmospheric (low negative) pressure was applied to the pleural space by water column. However, the right lung did not completely re-expanded.

Although reduced, bleeding restarted 24 h later. After re-attempting a conservative approach, on Day 14, a second surgical look was required with ongoing vv-ECMO. After surgical debridement and removal of the clotted blood, a full lung re-expansion was obtained. At the end of the surgery, independent lung ventilation was instituted as follow: the right lung was ventilated with high PEEP (ie 15 cmH₂O) and low (100 ml) tidal volume, whereas the left lung with lower PEEP (ie 8 cmH₂O) and a slightly higher (160 ml) tidal volume. This choice was indicated by the anesthesiologist based on different respiratory mechanics between right (low compliance and recruitable lung) and left (normal compliance). After 14 h, the right lung was completely recruited and lungs ventilated together, as described above.

2.3 | Infectious disease aspects

At ICU admission (Day 0), dexamethasone 6 mg daily was administered to the patient for the treatment of SARS-CoV-2 infection.⁵ The antibiotic therapy from the referring hospital was intravenous colistin 4.5 billion UI twice daily and vancomycin 2 g daily. Upon patient's arrival, extensively resistant Acinetobacter baumanii was isolated from blood culture, whereas a carbapenem -resistant Klebsiella pneumoniae strain from tracheal aspirate. Minimum inhibitory concentrations (MICs) were determined by broth microdilution according to Clinical and Laboratory Standards Institute (CLSI)⁶ and European clinical antimicrobial susceptibility testing (EUCAST)⁷ guidelines. The MIC of cefiderocol was determined by using disk diffusion test in according to the CLSI's recommendation. Antibiotic therapy was therefore continued with colistin, whereas vancomycin was switched to linezolid (600 mg twice daily). Given the low MIC for cefiderocol (0.047 µg/ml), antibiotic therapy with cefiderocol (2 g four times/day) was also instituted after ethics committee approval for compassionate use.⁸ After 7 days of treatment, blood cultures were negative for A. baumanii and cefiderocol was interrupted. Linezolid was also interrupted on Day 8.

On Day 11, a chest X-ray revealed new and progressive pulmonary infiltrates, concomitantly with worsening of respiratory mechanics, gas exchange, and hemodynamic status. After infectious disease consultation, aerosolized colistin 2.5 billion three times daily was started⁹ and continued till the improvement of the lung function (Day 24). Chest tubes were considered a potential infection source and removed with the aim to control the infection.

On Day 12, pharyngeal swab resulted negative for SARS-CoV-2.

After a transient improvement, a catheter-related bloodstream infection with septic shock due to *Candida parapsilosis* occurred on Day 20. Based on the manufacturer's instructions, identification and antifungal susceptibilities of candida isolate were determined using the VITEK 2 system (BioMerieux Italia SpA). Antifungal therapy was started initially with amphotericin B (3 mg/kg daily), then switched to caspofungin at 70 mg daily after 5 days, because of renal function impairment, until fungal infection resolution and ICU discharge (Day 41). On Day 58, the patient was discharged from the hospital and transferred to a rehabilitation center without need for long-term oxygen therapy.

3 | DISCUSSION

We report a case of a critical COVID-19 patient undergoing vv-ECMO for severe acute respiratory failure, requiring thoracic surgery and further complicated by sepsis. We believe that this challenging case had a favorable outcome thanks to a proactive and integrated, multidisciplinary approach.

COVID-19 is a disease leading to severe acute respiratory failure requiring mechanical ventilation in up to 15% of the patients² and vv-ECMO in up to 4%.¹⁰ In over 13% of patients undergoing mechanical ventilation, spontaneous pneumothorax may develop despite the use of protective mechanical ventilation and it increases the mortality by 14%.¹¹⁻¹³ The present case adds to the literature because of severity of the conditions, ie bilateral pneumothorax associated with right hemothorax (probably due to the concomitant needs for chest tube insertion and anticoagulation). Moreover, the deterioration of gas exchange required the attempt to run vv-ECMO, as rescue treatment. However, the continuous infusion of heparin could have precipitated the bleeding in such a fragile balance between bleeding and anticoagulation therapy for vv-ECMO. For this reason, we conducted a step-by-step strategy, mainly based on a conservative management and strict coagulation monitoring through TEG and the conventional blood tests to guide the administration of coagulation factors.¹⁴ In addition, the multidisciplinary meeting between thoracic surgeons and intensivists highlighted the increased risk of bleeding to run a thoracic surgery during vv-ECMO.¹⁵ The possibility to run vv-ECMO without therapeutic anticoagulation was considered, as widely described in several settings other than COVID-19.¹⁶ However, the hypercoagulative state of SARS-CoV-2 infection¹⁷ may have potentially and easily clotted the ECMO circuit with immediate major clinical adverse events, leading us to avoid a "heparin-free" strategy. In this complicated scenario, we collegially decided to attempt an initial conservative treatment with ongoing vv-ECMO and surgery only in case of failure. Although the 2014 ACC/AHA Guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery has recognized the anesthesiologist as the ideal "perioperative physician" to coordinate the preoperative evaluation,¹⁸ the importance of collegiality has been already reported in other thoracic surgery scenarios.¹⁹

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In ARDS patients, ventilator settings should be personalized according to different mechanical properties of the lung, in order to avoid de-recruitment and/or overdistension.²⁰ After the second surgical look, we faced with lungs at opposite mechanical properties: the right one with low static compliance (32 ml/cmH₂O), while the left one with suboptimal value (63 ml/cmH₂O). Therefore, in order to apply the best PEEP for two different lungs (to avoid alveoli collapse and/or overdistension) while guarantying a safe driving pressure, we successfully instituted an independent lung ventilation. Although could be considered a desperate measure, this technique has already been reported in patients with a lung abnormality that is predominantly unilateral.²¹

In COVID-19 patients, the risk of hospital-acquired infections is very high, with a probability of having an infection over 40% after 14 days of ICU stay. In the 35% of cases, infections are caused by multidrug-resistant bacteria, whereas fungal infections are less common.²² Although the use of a broad-spectrum therapy with one or more antimicrobials is strongly recommended in critically ill septic patients, Surviving Sepsis Guidelines also acclaim to narrow the therapy once pathogen is identified and sensitivities established.²³ In COVID-19 patients, the inappropriate use of antibiotics and overtreatment are very frequent, increasing the risk of adverse reactions including antibacterial resistance.²⁴ The excess of antibiotic use, without narrowing the therapy when evidence of resistant pathogens is lacking, is most of the time driven by the fear to miss the causative pathogen.²⁵ The antibiotic stewardship should be a core competency of critical care practitioners. A multiprofessional approach to antibiotic therapy, also including intensivists, infectious disease specialists and microbiology laboratory, is advisable to optimize ICU antibiotic management.²⁶ Although the risk and nature of secondary infections in COVID-19 patients are concerning, tractable targets for stewardship interventions exist, provided that a stewardship team is put in place and acts effectively.²⁷ We here optimized the antibiotic use by selecting antibiotic regimens with the highest level of effectiveness for the infection, through a multifaceted and multidisciplinary stewardship team.28,29 We also applied for compassionate use of cefiderocol for the treatment of extensively resistant Acinetobacter baumannii and carbapenem-resistant K. pneumoniae, based on our previous experience.⁸ As for the surgical strategy, the strict collaboration with the microbiology laboratory (to quickly identify the pathogens and sensitivities) and with the infectious disease specialists (to choose the best antibiotic therapy for the patient and to decide the best time to start and stop it) played a key role in the successful patient's management. Overall,

this case report suggests the importance of a multidisciplinary team acting proactively especially in critically ill patients affected by SARS-CoV-2 infection. The collegial approach to cares is fundamental in ICU for several aspects. During the COVID-19 pandemic, collegial decisional processes in limiting and withdrawing treatment have played a major role to allocate the scarce resources in priority to those patients with the highest probability of benefiting from intensive cares.³⁰ This holds true also before the pandemic: collegial and interdisciplinary meetings, together with several other factors, guide ICU physician in the decisions to limit or withdraw life support treatment in patients with limited intensive cares benefits.³¹ Collegiality is more and more important in the decision-making process to guide the best cares in the most severe and challenging cases. One of the most common situations of collegial approach is the acute kidney injury. Critically ill patients with acute kidney injury have increased morbidity and mortality. A personalized management, based on a multidisciplinary care team (ie physicians and nurses from different disciplines, as well as nephrologists and intensivists), is advisable in order to meet the needs of a critically ill patient.³² In the reported case, we have conducted a complex and multidisciplinary approach to health care, which involved not only intensivists and thoracic surgeons, but also infectious disease and microbiology physicians.

Whenever possible, sharing ideas, experiences, and knowledge among different specialists are fundamental, in order to quickly take the best decision for the patient, balancing benefits and risks, especially in particular conditions such as in our patient.

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CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

All authors made substantial contributions to patient's care. AB, EG, MM, AQ, EMT, GM, CT, and FL took part in the data acquisition, analysis, and interpretation, and they were involved in drafting the manuscript. AQ, GM, CT, and FL revised the manuscript for important intellectual content. All authors gave final approval of the version to be published and agreed to be accountable for all aspects

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of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

CONSENT

Signed consent for publication was obtained.

ETHICAL APPROVAL

Patient signed the informed consent modules and accepted the publication of clinical data for research and scientific purposes.

DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this paper.

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