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Rescue Venoarterial Extracorporeal Membrane Oxygenation After Cardiac Arrest in COVID-19 Myopericarditis: A Case Report

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ABSTRACT

Coronavirus Disease-2019 (COVID-19) has been associated with potentially life threatening cardiovascular complications, including fulminant myocarditis and cardiac tamponade. Optimal management strategies are still unclear, including the role of immunomodulatory therapies and extracorporeal membrane oxygenation (ECMO) in the context of cardiogenic shock. We report a case of a middle-aged female with COVID-19 who developed respiratory distress and hemodynamic deterioration with elevated troponin levels on the seventh day of symptoms. Echocardiography demonstrated pericardial effusion with diastolic restriction of the right ventricle. Cardiac arrest developed during pericardiocentesis, resulting in emergency thoracotomy and pericardial drainage. Venoarterial ECMO was subsequently initiated due to refractory cardiogenic shock. Tocilizumab, immunoglobulin, methylprednisolone and convalescent plasma were added to supportive care, with progressive recovery of cardiac function and successful weaning from mechanical ventilation. This case highlights the potential role of ECMO, convalescent plasma and immunomodulatory therapies in the management of cardiogenic shock associated with COVID-19 myopericarditis.

1. Introduction

Coronavirus Disease-2019 (COVID-19) has specific clinical characteristics which differentiate the condition from other respiratory viruses, especially regarding cardiovascular and thrombotic complications. Cardiac injury can occur in up to 28% of hospitalized patients and is associated with worse outcomes [1]. The role of extracorporeal membrane oxygenation (ECMO) in this scenario has yet to be clearly determined, since it has not been available in most healthcare facilities treating patients with COVID-19 around the World. Even in larger case series of hospitalized patients ECMO was rarely used, especially venoarterial [2]. We report a case of COVID-19 myopericarditis complicated by tamponade and cardiac arrest, successfully managed with venoarterial ECMO, convalescent plasma and immunomodulatory therapies.

2. Case report

A 45-year-old female with COVID-19, confirmed 3 days previously by nasopharyngeal swab testing, presented to the emergency department on May 10th, 2020 following a 7 day progression of dyspnea, fever, myalgia and postural hypotension. The patient had no previous comorbidities and denied any regular medications. On admission, heart rate was 125 bpm, blood pressure 105/72 mmHg, respiratory rate 26 breaths/min and oxygen saturation 100% on room air. Thoracic computed tomography confirmed bilateral pulmonary infiltrates compromising less than 25% of both lungs, in addition to pleural and pericardial effusions (Fig. 1A and B). Transthoracic echocardiography (TTE) demonstrated normal biventricular function, with moderate pericardial effusion and diastolic restriction of the right ventricle (Fig. 1C and D). Initial troponin I was 867 pg/mL (reference <34 pg/mL), and the remaining blood tests are shown in Table 1. Azithromycin, piperacillin/tazobactam and teicoplanin were initiated before admission to the intensive care unit (ICU).

Within 2 h of ICU admission, cardiac tamponade developed, necessitating urgent TTE-guided subxiphoid pericardiocentesis. The procedure was unsuccessful and 2 min after needle insertion, cardiac arrest in

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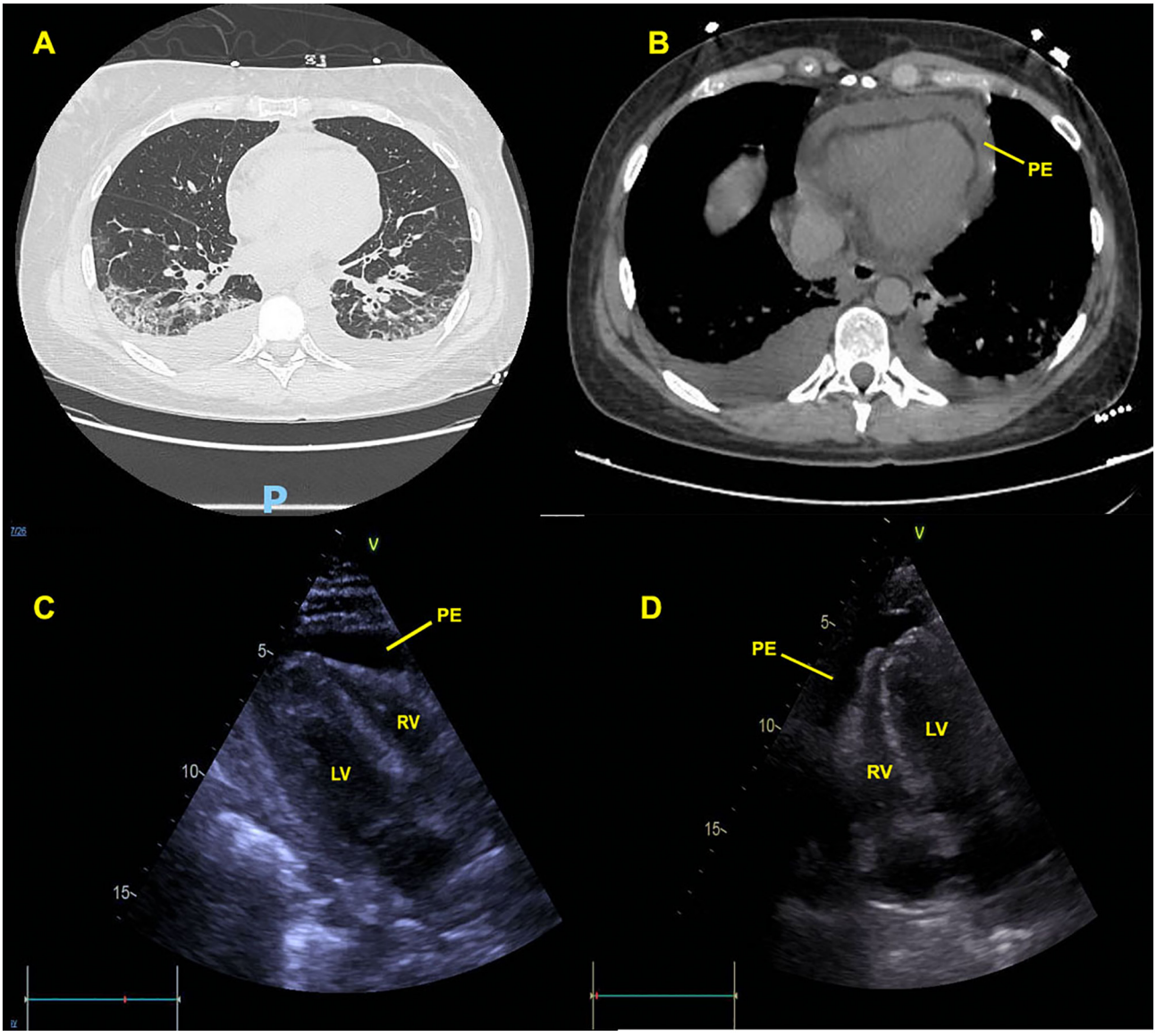

Fig. 1. (A) Computed tomography (CT) image showing pleural effusions and bilateral pulmonary infiltrates. (B) CT image showing pericardial effusion (PE). (C, D) Transthoracic echocardiography demonstrating PE and diastolic collapse of the right ventricle (RV).

asystole was diagnosed. Emergency thoracotomy was performed and followed by internal cardiac compression and pericardial drainage. The pericardial fluid was citrine yellow and no evidence of ventricular laceration was identified. Although spontaneous circulation was restored after 5 min, the patient progressed to refractory circulatory shock, despite the administration of noradrenaline, dobutamine, milrinone and vasopressin. New biventricular dysfunction was visualized on TTE and peak troponin levels reached 14,000 pg/mL.

Venoarterial extracorporeal membrane oxygenation (ECMO) was initiated 12 h after resuscitation through the left femoral vein and artery. Distal circulation was preserved by additional catheterization of the superficial femoral artery. Initial ECMO parameters were FiO_2 80%, rotation speed 2600 rpm, flow rate 4.3 L/min and sweep gas flow 3 L/min. Considering the possibility of fulminant COVID-19 myopericarditis, tocilizumab (400 mg single dose), immunoglobulin (1 g/kg/day for 2 days), convalescent plasma (1 unit) and methylprednisolone (750 mg and 250 mg on the first and second day, respectively, followed by 40 mg b.i.d.) were prescribed.

On the following day, haemodialysis was initiated and electroencephalography suggested a favourable prognosis after temporary reduction in sedation. Due to hemodynamic instability, neuroimaging was not performed. Peak interleukin-6 levels reached 933 pg/mL on May 14th and a second dose of tocilizumab was given, with an additional unit of convalescent plasma. Recurrent bleeding from the cannulation site resulted in the prescription of multiple blood products during hemodynamic support, despite rigours monitoring of unfractionated heparin (UFH) infusion.

Echocardiographic biventricular function progressively improved and ECMO was subsequently removed after 9 days, although residual right-sided dysfunction required continuation of dobutamine and milrinone during 3 additional days. Weaning from mechanical ventilation was achieved after appropriate management of pneumonia and successful extubation ensued on May 27th. Two weeks later, a pseudoaneurysm developed at the cannulation site and angioplasty of the femoral artery was necessary. Local soft tissue infection associated with *C. glabrata* and *C. parapsilosis* was also diagnosed, requiring surgical drainage and antifungal therapy.

Table 1
Laboratory findings on hospital admission. BNP - brain natriuretic peptide; LDH - lactate dehydrogenase.

Variable	Reference range	Value on admission
Hemoglobin, g/dL	12.0–15.5	16.2
Leukocyte count, cells/mm^3	3500–10,500	16,210
Basophil (%)		0.1
Eosinophil (%)		0
Neutrophil (%)		85
Lymphocyte (%)		11
Monocyte (%)		4
Platelet count, cells/mm^3	150,000–450,000	187,000
C-reactive protein, mg/dL	<0.5	2.1
LDH, U/L	120–246	256
Ferritin, ng/mL	6.2–137	478
Interleukin-6, pg/mL	1.5–7.0	16.9
D-dimer, ng/mL	<500	543
Troponin I, pg/mL	<34	867
BNP, pg/mL	<100	1840
Creatinine, mg/dL	0.5–1.0	0.8

Haemodialysis was interrupted on July 2nd and besides the development of critical illness myopathy, no further complications were identified. Discharge from the ICU occurred on July 4th, and was followed by further echocardiographic confirmation of complete biventricular recovery. Hospital discharge was given on July 15th with continuation of physiotherapy and voriconazole for 4 weeks.

3. Discussion

Heart failure has been diagnosed in up to 23% of patients with COVID-19, notably as a result of myocarditis, though pericardial involvement and tamponade have also been described [3,4]. While pericardiocentesis may be life-saving, subsequent management of respiratory insufficiency, myocardial dysfunction and circulatory shock can be challenging, since hemodynamic collapse is usually multifactorial [3]. Although circulatory support should be individualized, venoarterial ECMO may be a suitable choice when simultaneous respiratory and myocardial dysfunction are present.

In COVID-19, the risk of cardiopulmonary failure increases as systemic inflammation progresses. Hemodynamic support may be an important therapeutic component is these cases, though it is not available in the majority of healthcare facilities treating patients with COVID-19 around the World [1]. Most reports have been with venovenous ECMO, due to the predominant respiratory comprise. In a recent case series of 83 patients with COVID-19 managed with ECMO, only 2 were treated with venoarterial support [5]. As new knowledge continues to evolve in this area, case reports are relevant to provide the foundation for the development of additional research.

Few cases of fulminant myocarditis have been published in this context, and the benefit of ECMO remains uncertain, especially after recovery from cardiac arrest. Only 2 successfully treated cases of COVID-19 fulminant myocarditis and cardiogenic shock have been previously described, of which 1 was treated with venoarterial ECMO. Neither utilized tocilizumab or convalescent plasma as a management strategy. In addition, only 1 report of emergency ECMO cannulation after cardiac arrest in a patient with COVID-19 has been formerly documented, despite a subsequent unfavourable outcome [6].

In selected cases, ECMO may offer a possibility for spontaneous recovery and administration of immunomodulatory and supportive therapies, though the inherent risks associated with the procedure should be appreciated. Although patients seem to fare poorly in this scenario, our case is distinctive from previous descriptions because of the successful outcome. Selecting the appropriate moment to initiate ECMO is essential to ensure that the management strategy does not inflict a higher risk than the underlying disease. The identification of significant determinants of poor outcomes associated with ECMO support, such as older age, multiorgan failure, systemic comorbidities or severe respiratory compromise, is crucial to aid in clinical decision making in this setting [6]. In our case, though the post cardiac arrest neurological status was still uncertain, the absence of additional predictors of mortality and the early indication of hemodynamic support provided a favourable scenario for recovery of myocardial function.

Optimal management of anticoagulation during ECMO support in COVID-19 is unknown, particularly due to the increased thrombotic risk associated with the disease. Despite preliminary observational data suggesting higher prophylactic heparin doses in patients with COVID-19, it is unclear whether increasing UFH anticoagulation levels is associated with improved outcomes during ECMO support. Acquired antithrombin deficiency in this scenario can result in both thrombotic and haemorrhagic complications, which results in unpredictable net clinical effects associated with higher anticoagulation doses [2].

Harlequin syndrome could also be a concern, since pulmonary function in patients with COVID-19 may only recover over several weeks. Switching to venovenous ECMO or optimizing ventilator parameters before removing circulatory support are potential options. Furthermore, management of bleeding, secondary infections, renal failure and neurological complications are crucial components to achieve a successful outcome.

We describe the first case of fulminant COVID-19 myopericarditis and tamponade successfully treated with venoarterial ECMO, neutralizing antibodies and anti-inflammatory therapies, after recovery from cardiac arrest. Although stunned myocardium might have contributed to the cardiogenic shock, this complication tends to occur after longer periods of cardiac arrest and the subsequent recovery of ventricular function is often sooner than what was observed (<72 h) [7]. Supportive measures are still essential in this scenario, since evidence-based interventions are currently lacking.

Small case series have suggested promising results from COVID-19 convalescent plasma therapy, particularly in patients with Acute Respiratory Distress Syndrome (ARDS), regardless of cardiac involvement [3]. Duan et al. described a series of 10 patients with severe COVID-19 treated with 1 dose of convalescent plasma therapy, derived from recently recovered donors [8]. Within 3 days of plasma transfusion, significant clinical and laboratory improvement was observed, including an increase in oxygen saturation levels and lymphocyte count. No serious adverse effects were reported. In spite of these promising findings, the authors recognize the uncertainties regarding the optimal dose and timing of administration. The lack of a control group also limits the interpretation and generalizability of the results. Until further data from randomized clinical trials become available, evidence of efficacy will remain uncertain, particularly in uncommon presentations such as our case. Still, on August 20th, 2020 the Food and Drug Administration in United States issued an emergency use authorization for convalescent plasma from recovered patients to treat seriously ill COVID-19 infected individuals [9].

Even considering the possibility of subsequent fungal infections, as was observed in our case, interleukin-6 inhibitors may also have a favourable clinical effect in diminishing the disease's cytokine release syndrome [3,10]. Guaraldi et al. reported a retrospective analysis of 179 patients with severe COVID-19 treated with tocilizumab either intravenously or subcutaneously. After adjustment for a series of clinical variables, tocilizumab was associated with a significantly reduced risk of mechanical ventilation or death (adjusted hazard ratio 0.61, 95% CI 0.40–0.92; $p = 0.020$), although with a higher incidence of new infections (13% vs 4%, $p < 0.001$) [11]. Though tocilizumab has also been previously used without concomitant plasma therapy or ECMO in a recovered case of COVID-19 myocarditis, randomized trials are still necessary to clarify the exact role of interleukin-6 inhibitors in this context [12]. As such, it is difficult to estimate the influence of these interventions on our patient's outcome until additional research has been published.

4. Conclusion

Our report illustrates the importance of appropriate supportive measures in fulminant COVID-19 myopericarditis, particularly the potential role of timely venoarterial ECMO support for circulatory shock following recovery from cardiac arrest. Clinical risk stratification should be thoroughly performed in these cases to identify patients who may not benefit from the intervention. Further studies should also explore the effects of convalescent plasma transfusion and systemic immunomodulatory therapies in this scenario, regardless of the presence of ARDS.

Declaration of competing interest

The authors declare that there is no conflict of interest.

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