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CASE REPORT

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A case of COVID-19-associated fulminant myocarditis successfully treated with mechanical circulatory support

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Abstract

A 49-year-old man, who had not been vaccinated against COVID-19 visited the hospital for fever and cough, and a PCR test for COVID-19 was positive on the Day X. Initially, there was no decrease in oxygen saturation and the patient was under observation as a mild case without medication. Five days after the onset (Day X + 5), chest pain appeared. Electrocardiogram showed widespread ST-segment elevation, and blood tests showed high levels of troponin I. However, given that there was no stenotic lesion on coronary computed tomography, myocarditis was suspected, and he was transferred to our hospital on the Day X + 6. We started treatment with lemdesivir and dexamethasone. On the Day X + 7, the patient developed decreased left ventricular ejection fraction, hypotension, and hyperlactatemia. We decided that mechanical circulatory support was necessary and an Impella 5.0 was inserted under ventilator management. The patient was successfully weaned from the Impella 5.0 on the Day X + 17, was transferred to the general ward on the Day X + 24, continued rehabilitation, and was discharged home on the Day X + 39 with no heart failure symptoms. In this case, we performed daily bedside echocardiography and chose the Impella 5.0 instead of extra corporeal membrane oxygenation (ECMO) because there were no findings of severe pneumonia or right heart failure. The Impella 5.0 device was inserted via an axillary artery approach, given that it provides more assisted flow than the Impella CP inserted through the inguinal route. Furthermore, early rehabilitation was possible due to the lack of restriction of the lower body.

KEYWORDS

COVID-19, ECMO, fulminant myocarditis, impella, mechanical circulatory support (MCS)

1 | INTRODUCTION

Concurrent with the outbreak of infections caused by SARS-CoV-2, a novel coronavirus disease identified in 2019 (COVID-19), there have been scattered reports of myocarditis. Among them, fulminant myocarditis (FM) has been reported to account for 7% of COVID-19-related deaths.[1]

Although FM can cause sudden cardiac arrest and severe heart failure with unfortunate outcomes, it can be completely cured with appropriate management in the acute phase. Therefore, early diagnosis and treatment are important.

Among patients with FM, the first symptom is often cardiogenic shock. The recognition of this syndrome and its management with vasoactive medications and mechanical support has been extensively discussed in comprehensive reviews and scientific reports FM is a rare disease, and therefore, to date, there have been no randomized controlled trials evaluating the use of temporary mechanical circulatory support (MCS) devices. A few case reports have reported that full circulatory support and perfusion of the patient's end organs, thereby allowing time for cardiac recovery were effective.[2]

In the present study, we report a case of COVID-19-related FM in a healthy middle-aged man without underlying conditions who had a good outcome after MCS with an Impella 5.0. This case is the first in the literature in which the Impella 5.0 was used for MCS without extra corporeal membrane oxygenation (ECMO) in COVID-19-related FM.

2 | CASE DESCRIPTION

The patient was a 49-year-old man, 187 cm tall, 65 kg in weight, with a Body Mass Index (BMI) of 18.6. He visited his family doctor with symptoms of a common cold, fever, and cough, and a Polymerase Chain Reaction (PCR) test positive for COVID-19 on the Day X. No decrease in oxygen saturation was observed, and he was admitted for follow-up as a mild case.

On Day X + 5, the sixth day of onset and hospitalization, the patient became aware of chest pain and developed hypotension with a systolic blood pressure of 80 mm Hg. Blood tests showed elevated troponin I levels, and an electrocardiogram (ECG) showed widespread ST-segment elevation (Figure 1A), for which he was suspected of having myocarditis. The patient was transferred to our intensive care unit (ICU) for multidisciplinary care on the Day X + 6. Blood tests trends and serological tests for various viruses are shown in Table S1.

Vital signs on admission were heart rate 120 bpm, blood pressure 80/50 mm Hg, oxygen saturation (SpO_2) 99%, under oxygen supplementation 6 L/min, consciousness state of 15 points on the Glasgow Coma Scale (GCS), and body temperature of 36.1°C. The physical examination revealed coldness and sweating of the extremities, which were suggestive of shock. Echocardiography showed severe edema of the left ventricular (LV) wall and decreased left ventricular wall motion with a left ventricle ejection fraction (LVEF) of 30%. There were no findings suggestive of

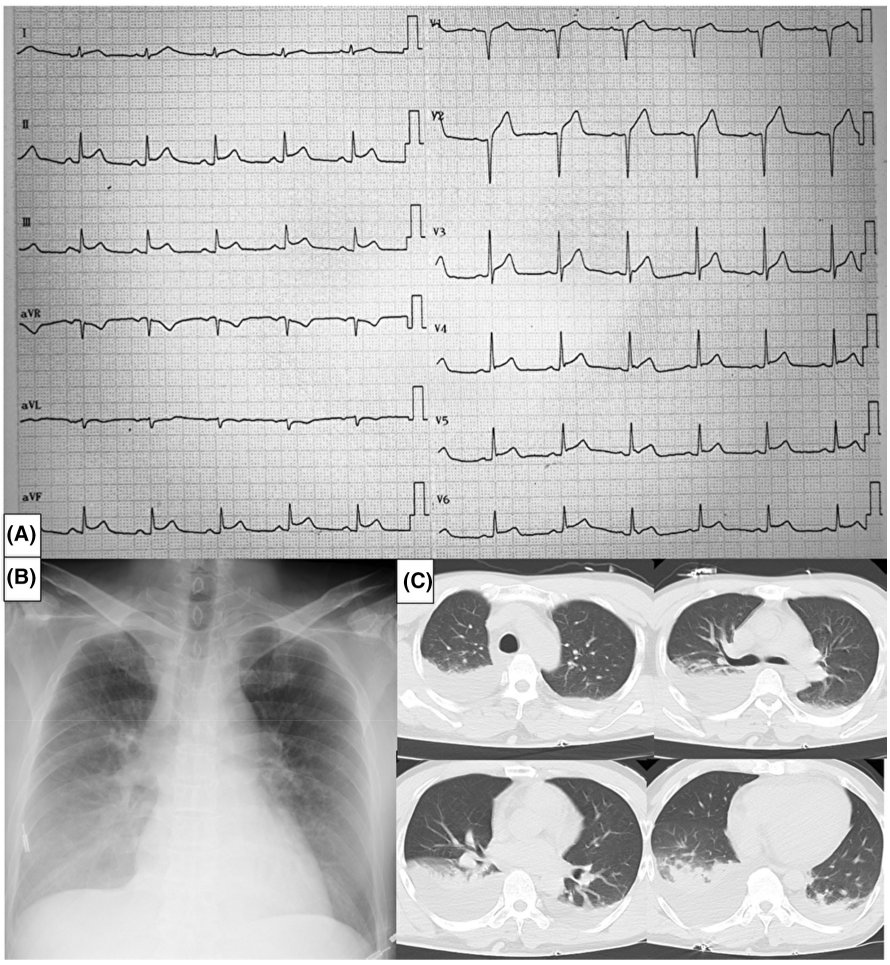

FIGURE 1 (A) Electrocardiogram. Diffuse and concave ST elevation with PR-segment depression. (B) Chest X-ray on the Day X + 6. Infiltrative shadow in the pulmonary hilar region. (C) Chest CT images on the Day X + 6. Bilateral pleural effusions, but no findings suggestive of pneumonia such as diffuse glass opacity (GGO) with peripheral predominance

hypovolemic shock, and there were no abnormalities in thyroid hormone levels. Blood bacterial culture was negative.

Chest Computed Tomography (CT) scan showed bilateral pleural effusions, but no typical findings of COVID-19 pneumonia (Figure 1C). Coronary CT scan showed no stenosis of the coronary arteries. After consulting with cardiologists, we strongly suspected myocarditis rather than acute coronary syndrome (ACS) because this patient had no coronary risk factors such as diabetes, hypertension, or smoking, widespread ST-segment elevation was mild and there was no stenosis on coronary CT. In addition, we decided not to perform coronary catheterization due to the risk of exposure to COVID-19 infection in the angiography room. We started the patient on remdesivir and dexamethasone for COVID-19. Noradrenaline and dobutamine were also used for cardiogenic shock (Figure 2).

However, the patient's condition worsened on Day X + 7, the eighth day of onset. Given that the echocardiographic evaluation showed that LVEF had decreased to less than 20% and lactate levels had not improved, we determined that mechanical circulatory support was necessary. Echocardiography showed decreased left ventricular contraction and marked edema, but right heart function was within normal limits with tricuspid annular plane systolic amplitude of 18.7 mm, systolic wall motion velocity of 11.8, and right ventricular (RV) fractional area change of 39%. There were no findings suggestive of pulmonary hypertension such as septal flattening or right ventricular enlargement. In addition, pulmonary CT showed no typical findings of COVID-19 pneumonia, and the PaO_2/FiO_2 (P/F) ratio was over 200. The hemodynamic status was judged to involve inadequate ejection from the left ventricle, and circulatory support with an Impella 5.0 was selected instead of ECMO. In addition, we were prepared to add ECMO if right heart failure became apparent. Adequate sedation was deemed necessary, and the patient was intubated and placed on a ventilator. The Impella 5.0 was inserted into the left ventricle through the axillary artery by a cardiac surgeon. Immediately after insertion, echocardiographic findings showed an LVEF of less than 10% and almost no self-cardiac output; the patient was judged to have FM and steroid pulse therapy with methylprednisolone 1000 mg/day for 3 days was initiated.

Circulatory support with the Impella 5.0 reached P8 (flow rate 4.5 L/min) at one point, but the support volume was decreased as LVEF recovered (Figure 2, Appendix S1A–C), and echocardiography confirmed recovery of left ventricular wall motion (Appendix S1D). The patient was weaned on the Day X + 17. His lung condition was good, and the ventilator could be managed with minimal settings throughout (PEEP 5–8 cmH_2O, pressure support 5 cmH_2O, P/F ratio 300–400). The steroid dose was tapered and discontinued on the Day X + 22.

Cardiac magnetic resonance imaging (MRI) performed on the Day X + 29 showed mild late gadolinium enhancement (LGE) on the epicardial side of the inferior wall of the heart base, mild high signal on T2-weighted MRI of the same area, mild high signal on T1-weighted MRI, mild fibrosis, and edema-like changes (Figure 3). A myocardial biopsy was performed on the Day X + 35. Pathological findings showed mild myocyte hypertrophy, some subendocardial fibrosis, and scattered Cluster of Differentiation 3 (CD3)-positive T cells (Figure 4B), but no thrombus, myocardial necrosis, or complex arrangement (Figure 4A). The patient was discharged home on the Day X + 39 with no symptoms of heart failure and no medication. The patient has been reintegrated into society and is currently under observation at a local hospital.

3 | DISCUSSION

The mechanism of myocarditis caused by COVID-19 is currently thought to be a combination of direct cytotoxicity through cytokine release and the ability of the virus to bind to the ACE2 spike protein on cardiomyocytes and induce injury.[3]

In previous studies, pathological myocardium findings in COVID-19 showed fewer lymphocyte-dominated inflammatory infiltrates associated with myocardial cell damage than are usually seen in viral myocarditis.[4] Due to the lack of clear histopathological findings to diagnose these patients, the diagnosis of COVID-19 myocarditis is determined by cardiovascular magnetic resonance (CMR) in 60% of the cases.[5] European Society of Cardiology (ESC) guidelines state that CMR, if available, is preferred method for diagnosis of acute myocarditis. Endomyocardial biopsy is not recommended for the routine assessment of patients suspected of having COVID-19 myocarditis and should be limited to cases of severe or refractory heart failure where histological findings may guide therapeutic choices.[6]

The American Heart Association (AHA) recommends the use of cardiac imaging modalities such as echocardiography and CMR for patients with signs of suspected myocarditis.[2] In particular, echocardiography is portable and can be more easily introduced.[3]

In the ICU, daily echocardiographic and pulmonary echocardiographic assessments provided useful support for treatment planning and our decisions to adjust or wean off mechanical circulatory support were based on the patient's improved hemodynamic and echocardiographic findings.

Cardiovascular magnetic resonance could not be performed during the acute phase or ICU stay but was performed 23 days after onset. It showed mild LGE on the epicardial side of the inferior wall of the cardiac base, and mild high signal on T2-weighted MRI of the same area.

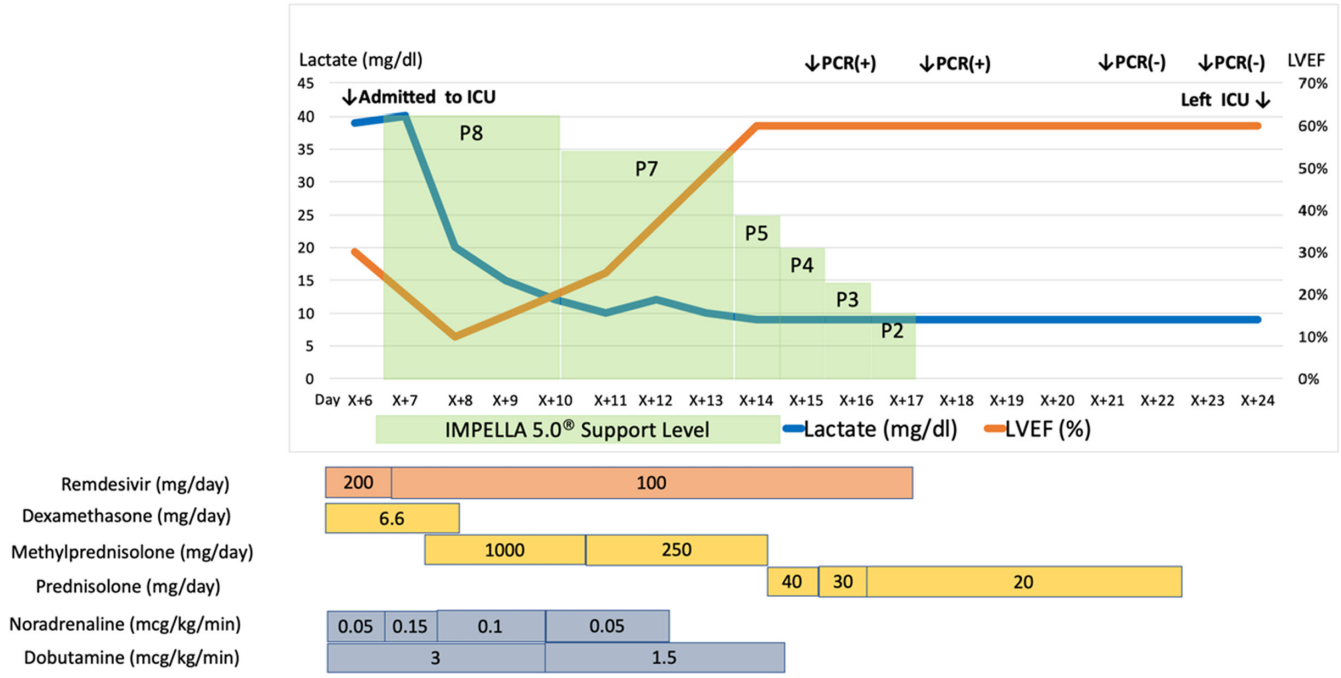

FIGURE 2 Clinical course

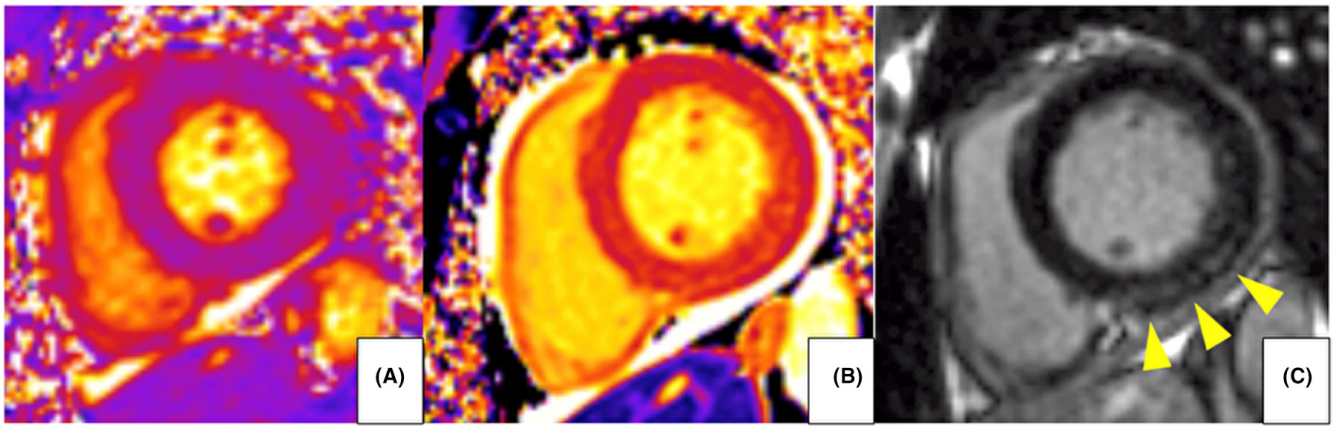

FIGURE 3 CMR. (A) T2 map. (B) native T1 map. (C) late gadolinium enhancement (LGE). CMR showed a slight increase in T2 map values (45 ms vs. 43 ms in remote myocardium) and native T1 values (1303 ms vs. 1301 ms in remote myocardium) in the basal-septum and basal-lateral segments. In these segments, the LGE sequence showed subepicardial enhancement, as shown by the yellow arrow heads

CMR has high diagnostic value for the diagnosis of patients suspected of having acute myocarditis according to 2018 Lake Louise Criteria.[7]

On the contrary, there are no clear recommendations for the treatment of SARS-CoV-2 associated myocarditis.[3] The applicability of remdesivir and dexamethasone for patients with myocarditis in severe COVID-19 pneumonia is still unknown.[8,9] MCS, inotropes and/or vasopressors, and mechanical ventilation can be needed in severe cases. There is no compelling evidence to support the use of immunomodulatory therapy such as corticosteroids and intravenous immunoglobulins. However, corticosteroids are indicated when there is respiratory involvement and have been administered to patients who then had favorable clinical outcomes. Tocilizumab and favipiravir are currently being tested in a randomized trial.[6]

In this case, we chose remdesivir and dexamethasone as the treatment of choice for COVID-19, and steroid pulse therapy as the treatment for fulminant myocarditis. As a result, the patient was discharged with a favorable clinical course.

For treatment of circulatory failure, MCS such as ECMO, assisted ventilation, and intra-aortic balloon pumps are options for patients who do not respond to standard therapies. Several previous case reports have shown successful results using the Impella for the treatment of severe myocarditis

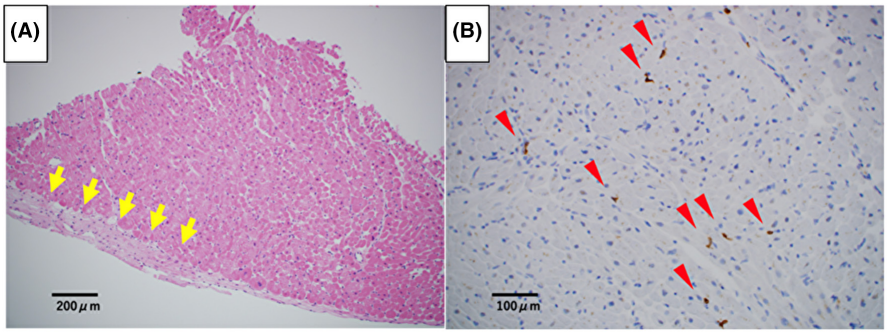

FIGURE 4 Pathological image. (A) Yellow arrows indicates mild fibrosis in the subendocardium. (B) Red arrow heads indicates CD3-positive T cells which infiltrated in myocardium

and cardiogenic shock, either in combination with ECMO (ECMELLA) or in combination with RV-Impella RP (BI-PELLA) as the only means of circulatory support.[10–14] On the contrary, some reports of patients with fulminant myocarditis who were not infected with COVID-19 have had successful outcomes with brief use of LV-Impella in patients who did not have significantly impaired RV function and did not require biventricular support.[15–18]

This case is one of the first in which the Impella 5.0 was used alone for SARS-CoV-2 associated myocarditis. We used the Impella 5.0 instead of ECMO because there were no indications of severe pneumonia or right ventricular failure. Fortunately, our patient recovered quickly without any complications. We believe that the main reason for this success was the choice to use the Impella 5.0.

The Impella 5.0 is capable of maintaining incremental blood flow, which allows for sufficient cardiac output to ensure organ perfusion. It also reduces the left ventricular afterload and allows the left ventricle to rest. In this case, the patient temporarily had very little cardiac output of his own and required support at the P8 level (flow rate of 4.5 L/min). If we had chosen the Impella CP (maximum flow rate of 3.7 L/min), we might not have been able to achieve adequate perfusion. The absence of severe pneumonia or right ventricular failure was also an important factor. Had they been present, ECMO would have been necessary; ECMO was on standby, but we never had the need to use it. Another advantage of choosing the Impella 5.0 was that it could be inserted through the axillary artery, so there was no restriction of movement in the lower body, which would have interfered with rehabilitation.

In this case, rehabilitation was performed from the third day of Impella introduction, and the patient was able to return to society smoothly without complications of disuse syndrome.

4 | CONCLUSION

We chose a unique approach to the management of a case of COVID-19-related fulminant myocarditis. This report is the first on the use of the Impella 5.0 for circulatory support without concomitant ECMO. This choice of treatment ensured an adequate ejection fraction and early rehabilitation which saved the patient. To select an appropriate device, it is important to repeatedly check the clinical status and carefully monitor the right and left cardiac functions by echocardiography.

AUTHOR CONTRIBUTIONS

RA was the attending physician and wrote the draft manuscript; TK was a member of the treatment team and mainly managed Impella; MO was a member of the treatment team and completed the paper; MO is also the corresponding author. NK is the supervising physician in the ICU and has full responsibility for treatment. All authors interpreted clinically and took part in the discussion during manuscript preparation.

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FUNDING INFORMATION

None.

CONFLICT OF INTEREST

There are no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

None.

ETHICAL APPROVAL

None.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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