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CASE REPORT

ADVANCED

HEART CARE TEAM/MULTIDISCIPLINARY TEAM LIVE

Fulminant Giant Cell Myocarditis Requiring Bridge With Mechanical Circulatory Support to Heart Transplantation

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ABSTRACT

Giant cell myocarditis is a rare cause of cardiogenic shock requiring a high index of suspicion, rapid immunosuppressive therapy, and mechanical circulatory support. We present the case of a patient with giant cell myocarditis who underwent a successful bridge with four different types of mechanical circulatory support devices to heart transplantation. (**Level of Difficulty: Advanced.**) (J Am Coll Cardiol Case Rep 2022;4:265-270) © 2022 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Giant cell myocarditis (GCM) is a rare cause of cardiogenic shock requiring a high index of suspicion, rapid immunosuppressive therapy, and mechanical circulatory support. We present the case of a patient with GCM based on clinical presentation, who had a delay in pathologic diagnosis amid the COVID-19 pandemic, but eventually underwent successful bridge with four different types of mechanical circulatory support devices to orthotopic heart transplantation (OHT).

LEARNING OBJECTIVES

- To recognize giant cell myocarditis as a cause of cardiogenic shock resulting from biventricular heart failure and ventricular arrhythmias.
- To engage the multidisciplinary team in the decision pathways for escalation of mechanical circulatory support to preserve end-organ function and improve survival.

CASE PRESENTATION

Our patient is a 69-year-old woman with nonischemic dilated cardiomyopathy and a left ventricular ejection fraction (LVEF) of 35%, who recovered her LVEF with guideline-directed medical therapy and cardiac resynchronization therapy. She now presented with 1 week of fever, chills, diarrhea, and worsening dyspnea. There were signs and symptoms of shock and end-organ hypoperfusion.

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ABBREVIATIONS AND ACRONYMS

ECMO = extracorporeal membrane oxygenation

GCM = giant cell myocarditis

LVAD = left ventricular assist device

LVEF = left ventricular ejection fraction

OHT = orthotopic heart transplantation

PA = pulmonary artery

RA = right atrium

RV = right ventricle

QUESTION 1: WHAT IS THE DIFFERENTIAL DIAGNOSIS AND WHAT IS THE DIAGNOSTIC APPROACH?

Differential diagnoses included acute coronary syndrome, fulminant myocarditis, septic shock, COVID-19 infection, acute pulmonary embolism, and acute aortic syndrome. The initial workup revealed a negative result of SARS CoV-2 polymerase chain reaction testing and an elevated Coxsackie B virus titer to 1:320. The transthoracic echocardiogram demonstrated LVEF of 20%, severe right ventricular (RV) dysfunction, and severe mitral regurgitation. A right heart catheterization revealed a right atrial (RA) pressure of 6 mm Hg, RV pressure of 32/9 mm Hg, pulmonary artery (PA) pressure of 30/20/25 mm Hg, pulmonary capillary wedge pressure of 22 mm Hg with V waves of 30 mm Hg, left ventricular end diastolic pressure of 32 mm Hg, cardiac output of 3.3 L/min, and cardiac index of 1.95 L/min/m^2. An electrocardiogram revealed markedly low voltage and ventricular paced rhythm (**Figure 1**). A coronary angiogram revealed nonobstructive coronary artery disease.

QUESTION 2: WHEN SHOULD GCM BE SUSPECTED AND HOW IS THE DIAGNOSIS ESTABLISHED?

Acute cardiogenic shock and incessant ventricular arrhythmia raise the clinical suspicion for GCM. However, the presentation can vary in severity, and maintaining a high clinical suspicion is imperative to establishing a correct diagnosis. An early endomyocardial biopsy can establish the diagnosis and lead to the implementation of therapy.[1,2]

Endomyocardial biopsy is limited by sampling error and lacks the sensitivity to definitively rule out GCM, as occurred in our patient.[3] Considering a worsening cardiovascular status and with positive viral titers, there was a high suspicion for myocarditis. Therefore, our patient underwent a cardiac biopsy on hospital day 12 and was treated with empiric high-dose steroids with 1 g methylprednisolone. The endomyocardial biopsy results were nondiagnostic.

QUESTION 3: WHAT IS THE PATHOPHYSIOLOGY OF GCM AND WHAT ARE THE OPTIONS FOR MEDICAL THERAPY?

The cause of GCM is unclear, but it is characterized by inflammatory infiltration of the myocardium by T-lymphocytes and macrophages.[2] Some autoimmune disorders and viral myocarditis have been associated with GCM; however, the direct link to pathogenesis is limited.[2] Our patient had evidence of Coxsackie B virus on presentation, but it is not clear whether this was pathologically linked in this case.

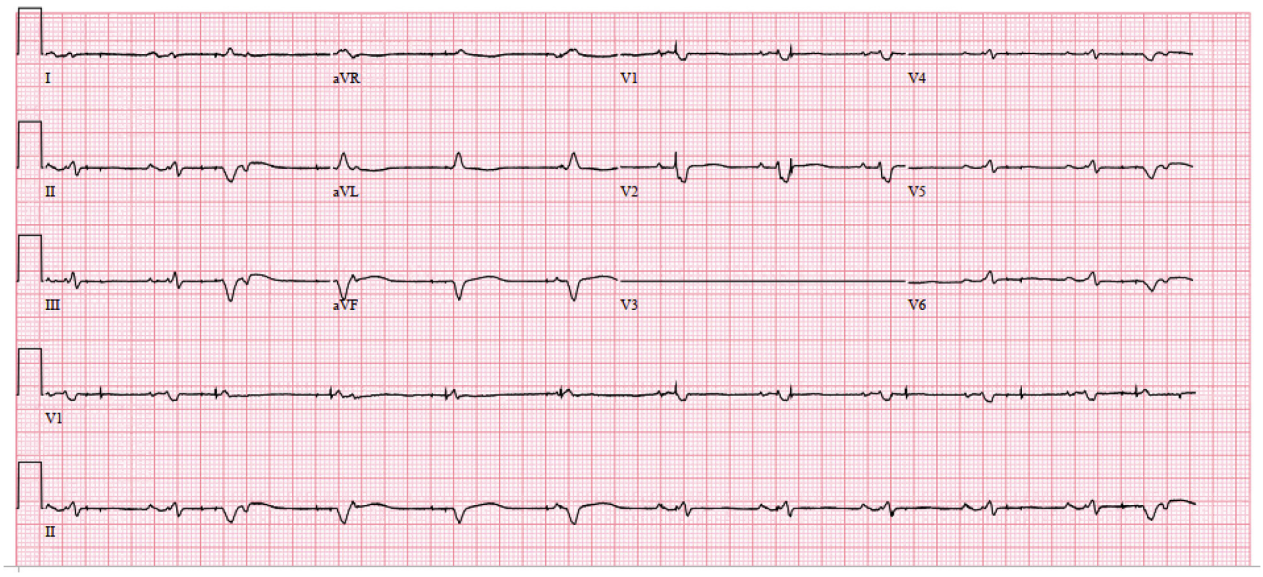
Immunosuppression is the cornerstone of medical management of GCM. However, ideal immunosuppression is not known because of the scarcity of high-quality data.[2] Management usually involves two- or three-drug regimens with corticosteroids, a calcineurin inhibitor (cyclosporine or tacrolimus), azathioprine, or mycophenolate mofetil. Alternatively, more aggressive management with an antithymocyte globulin or alemtuzumab have also been used.[2] The impact of immunotherapy before transplant is unknown, and a significant proportion of patients experience progression despite medical management.[3,4]

QUESTION 4: WHAT ARE THE OPTIONS FOR TEMPORARY MECHANICAL CIRCULATORY SUPPORT FOR CARDIOGENIC SHOCK AND WHICH SUPPORT IS MOST APPROPRIATE FOR OUR PATIENT?

The choice of support depends on the severity of cardiogenic shock, the underlying cause of the shock, the chambers involved, and the amount of support required. It is imperative determine the chambers involved: either left ventricle or RV or both. There are four basic configurations for support: 1) drainage from the right atrium (RA)/inferior vena cava/superior vena cava and return to the systemic arterial system; 2) drainage from the LA and return to the systemic arterial system; 3) drainage from the LV and return to the aorta; and 4) drainage from the inferior vena cava/superior vena cava/RA and return into the PA. The device chosen after a multidisciplinary discussion will provide different amounts of support from 0.5 to 10 L/min. The LV support includes intra-aortic balloon pump, LV-aortic microaxial pump, or extracorporeal membrane oxygenation (ECMO). RV support may be provided percutaneously with a microaxial RA-PA pump or an extracorporeal RA-PA pump. Biventricular support may be established with ECMO or a surgical extracorporeal pump with central cannulation, and by various other combinations.

Although the RV is often involved with myocarditis, the multidisciplinary team decided to proceed with left-sided support alone because of the normal RA pressure at the time of RHC. Inasmuch as recovery in these patients is often prolonged, we opted for an axillary LV-aortic microaxial pump, which can maintain support over days to weeks while permitting

FIGURE 1 **Electrocardiogram**



Hospital day 15, marked low voltage, V-paced.

patients to ambulate if possible. The patient's hemodynamics stabilized briefly, but soon afterward, she experienced worsening shock with acute kidney and liver injury and incessant ventricular tachycardia/fibrillation requiring multiple shocks. She was treated with intravenous lidocaine, amiodarone, and procainamide drips. Because of the critical cardiogenic shock with refractory arrhythmias, the support was escalated to venoarterial-ECMO in addition to an axillary LV-aortic microaxial pump on hospital day 14 (**Figure 2**).

With that support, analysis of the patient's hemodynamics revealed an RA of 11 mm Hg, PA of 22/18/19 mm Hg, pulmonary capillary wedge pressure of 20 mm Hg, and a mixed venous saturation of 78% with 4 L of ECMO flow and 1.4 L of LV-aortic pump flow on the P4 setting. Given the patient's refractory cardiogenic shock and continued electrical instability, she was transferred to the hospital day 15 for consideration of durable mechanical support or OHT. After a preliminary evaluation revealed no major contraindications to heart transplantation, the team opted to continue with the temporary mechanical circulatory support while the transplantation evaluation was rapidly completed. However, there was concern about low PA pulsatility precipitating thrombus formation in the pulmonary arteries; therefore, a PA outflow cannula was added through the right internal jugular vein to maintain flow in the PA (**Figure 2**). However, she experienced refractory arrhythmias that were associated with progressive multiorgan system dysfunction. To provide higher flows while also ensuring complete decompression of both sides of the heart, we decided to escalate her mechanical circulatory support to a surgical temporary biventricular assist device with an oxygenator and with drainage cannulas in RA and LV apex and reinfusion cannula in the ascending aorta (**Figure 2**).

QUESTION 5: WHAT ARE THE SURGICAL OPTIONS FOR GCM?

Mechanical circulatory support and heart transplantation are often the ultimate therapies for severe GCM. Montero et al.[5] describe the French experience of using mechanical circulatory support in 13 patients with severe GCM, 85% of whom required veno-arterial ECMO support. Four patients died while using mechanical circulatory support, and nine underwent OHT.[5] In a recent systematic review, Patel et al[6] described the outcomes in patients with GCM who required mechanical circulatory support. The authors found that similarly to our case, the vast majority of patients (76.7%) required biventricular support, and 58.5% underwent OHT.[6] Ma et al[7] recently described a similar case of a patient with fulminant GCM, requiring biventricular support. Unlike the patient in

FIGURE 2 Hospital Course

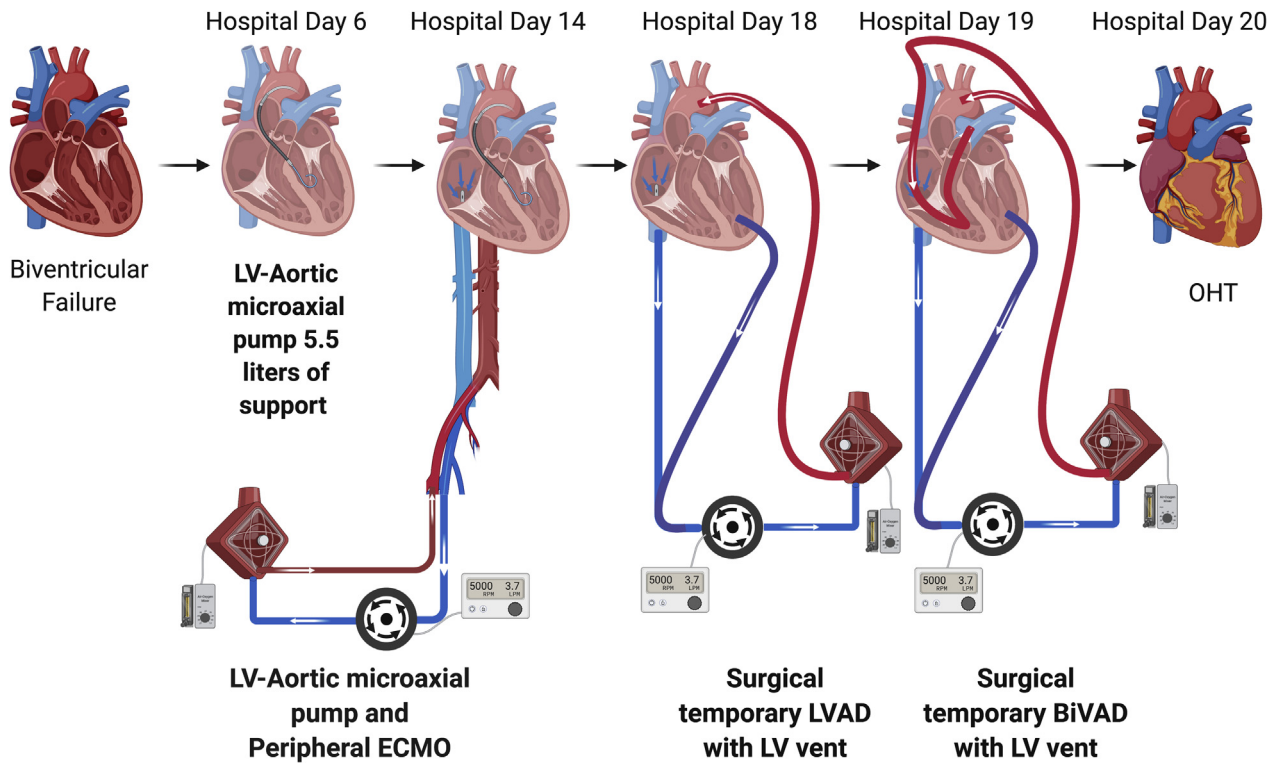


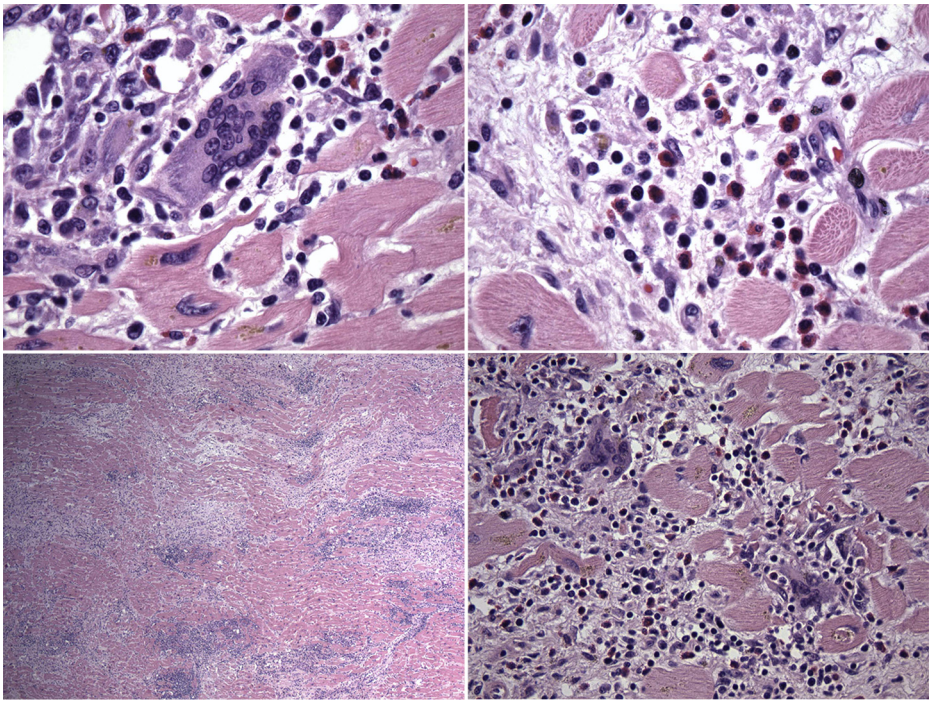
Figure was created with Biorender.com. BiVAD = biventricular assist device; ECMO = extracorporeal membrane oxygenation; LVAD = left ventricular assist device.

our case, their patient was significantly older and was not a candidate for OHT or durable VAD. The patient was successfully treated with antithymocyte globulin and pulse-dose intravenous methylprednisolone, and underwent transition away from mechanical circulatory support and was discharged with maintenance immunosuppression.[7] Patel et al[8] described another case of a young man with fulminant GCM who required temporary biventricular support with an LV-aorta pump and an RA-PA pump. The patient was eventually able to undergo transition to a durable left ventricular assist device (LVAD) without RV support.[8] Fallon et al[9] described a more indolent course in a patient with progressive heart failure treated for presumed GCM over a 10-year period. Their patient was treated with immunosuppression and durable LVAD as a bridge to a successful OHT.[9] These cases highlight the wide range of acuity of presentations in patients with GCM and the need for up-front aggressive therapy in most cases.

Unfortunately, the available data on GCM are limited to case reports and small case series. The outcomes in patients presenting with a severe form of GCM are poor, and these patients are often not responsive to medical management alone. Fundamental to the successful treatment of our patient with severe cardiogenic shock was early reassessment after each intervention and the ability to quickly transition to a higher level of mechanical circulatory support when needed. In particular, we needed to address the limitation of peripheral venoarterial-ECMO to maintain adequate flow in the PA when RV function is extremely poor or refractory arrhythmias are present. In these situations, it is sometimes necessary to switch to surgical ventricular assist devices to provide adequate decompression of the ventricles while maintaining appropriate levels of systemic flow.

Our patient underwent expedited evaluation for durable mechanical circulatory support and OHT. On hospital day 18, she was urgently listed for OHT for cardiogenic shock with surgically implanted VAD support. On hospital day 20, she underwent OHT without complications. Her immediate postoperative support included dobutamine 10 μg/kg/min, norepinephrine 2 μg/min, inhaled nitric oxide 20 ppm, but no mechanical circulatory support. Vasopressors,

FIGURE 3 Heart Explanted Pathological Specimen



Massive myocarditis with an infiltrate predominantly of lymphocytes, numerous mononuclear cells, scattered eosinophils, and multinucleate giant cells. Extensive healing fibrosis, which appears to be approximately 2 weeks old.

inotropes, and inhaled nitric oxide were successfully weaned by postoperative day 3, and she was extubated by postoperative day 4. Pathologic examination of the explanted heart was consistent with GCM (Figure 3).

CONCLUSIONS

We describe the case of a patient with fulminant GCM who presented with severe cardiogenic shock, electrical instability, and end-organ damage. Nondiagnostic initial endomyocardial biopsy is not enough to rule out the disease when clinical suspicion is high. The expertise of the multidisciplinary team approach with heart failure, electrophysiology, interventional cardiology, cardiothoracic surgery, infectious disease, and intensive care is often needed to provide care in a complex clinical scenario like that of the patient we describe. The rapid escalation of support devices is warranted in fulminant cases to preserve end-organ function and improve survival.

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