JACC: CASE REPORTS VOL. 2, NO. 10, 2020

MINI-FOCUS ISSUE: HEART FAILURE

INTERMEDIATE

CASE REPORT: CLINICAL CASE

Biventricular Intravascular Microaxial Blood Pumps and Immunosuppression as a Bridge to Recovery in Giant Cell Myocarditis

Janet I. Ma, MD,[a] Enrico Ammirati, MD, PhD,[b] Michela Brambatti, MD, MS,[a] Eric Adler, MD[a]

ABSTRACT

We report a case of giant cell myocarditis in a 76-year-old patient managed with combined immunosuppression and biventricular intravascular microaxial blood pumps. This case highlights a feasible approach for managing such patients who are not candidates for transplantation or durable ventricular assist devices. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2020;2:1484–8) © 2020 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/).

PRESENTATION

A 76-year-old man presented to his local emergency department with weakness and presyncope. He recently developed upper respiratory symptoms after a vacation in Vietnam. Upon admission, he was afebrile with heart rate of 126 beats/min, blood pressure of 80/50 mm Hg, and normal oxygen saturation. The physical examination was notable for findings of cool extremities, elevated jugular venous pressure, and weak pulse.

LEARNING OBJECTIVES

- To maintain a high clinical suspicion for GCM and perform EMB at an early stage of presentation in patients of any age.
- To consider prolonged temporary MCS for GCM patients who are not candidates for transplantation or durable MCS.

MEDICAL HISTORY

The patient had a medical history of pituitary adenoma status post-resection with subsequent panhypopituitarism. His personal and family history were negative for cardiovascular, autoimmune, or rheumatologic disease.

DIFFERENTIAL DIAGNOSIS

The initial differential diagnosis included cardiogenic shock (acute coronary syndrome, cardiac tamponade, acute decompensated heart failure [HF], fulminant myocarditis), pneumonia with septic shock, or distributive shock due to adrenal insufficiency, pulmonary embolism, and acute aortic syndromes.

From the [a]Division of Cardiology, Department of Medicine, University of California, Sulpizio Cardiovascular Center, San Diego, California; and the [b]Transplant Center and De Gasperis Cardio Center, Niguarda Hospital, Milano, Italy. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Case Reports* author instructions page.

Manuscript received November 1, 2019; revised manuscript received April 28, 2020, accepted May 13, 2020.

ISSN 2666-0849 https://doi.org/10.1016/j.jaccas.2020.05.107

INVESTIGATIONS

Troponin I concentration was 26.9 ng/ml, rising to 144.4 ng/ml (normal values are 0.00 to 0.09 ng/ml). B-type natriuretic peptide (BNP) was 2,092 pg/ml (normal values are 0 to 99 pg/ml). Initial transthoracic echocardiogram (TTE) showed left ventricular ejection fraction (LVEF) of 30%. Coronary angiography showed no obstructive disease.

MANAGEMENT

The following day, he had multiple ventricular tachycardia arrests requiring shocks and intubation. He also developed third-degree atrioventricular block prompting temporary pacer wire placement. An intravascular microaxial blood pump (Impella 5.0, Abiomed, Danvers, Massachusetts) was placed in the left ventricle, and he was transferred to the authors' hospital for evaluation of heart transplantation. His vital signs upon transfer showed a heart rate of 110 beats/min and a blood pressure of 75/60 mm Hg, despite multiple inotropic and vasopressor agents (**Table 1**). On physical examination, he was intubated and sedated with mildly elevated jugular venous pressure and no lower extremity edema. He was noted to have ventricular tachycardia requiring lidocaine and mexiletine. A second TTE showed biventricular failure with LVEF dropping to 10% to 15%, prompting placement of a right ventricular intravascular microaxial blood pump (Impella RP, Abiomed) (**Figure 1A**). He was also urgently placed on continuous venovenous hemofiltration for anuria. An endomyocardial biopsy (EMB) was performed and histology confirmed giant cell myocarditis (GCM) (**Figure 1B**). Given his age and severe biventricular HF, he was not a candidate for heart transplantation. He was not a candidate for a durable left ventricular assist device due to his right ventricular dysfunction and renal failure. He was treated with 1 dose of rabbit anti-thymocyte globulin (1 mg/kg), pulse-dose intravenous methylprednisolone (1 g/day for 3 days with rapid tapering in the following days to stress dosages given the presence of panhypopituitarism); cyclosporine, 50 mg twice daily (with a blood concentration goal of 200 to 300 ng/ml); and azathioprine, 50 mg daily. Tracheostomy was performed on hospital day 6. The transvenous pacer was removed on hospital day 12 with complete resolution of ventricular tachycardia (**Figure 1C**) and heart block and recovery of sinus rhythm (**Figure 1D**). Right-sided mechanical circulatory support (MCS) was removed on hospital day 14, with complete recovery of right ventricular function on repeated TTEs. Due to reactivation of a cytomegalovirus (CMV) infection (7 million copies/ml) with tracheitis, colitis, and worsening transaminitis, his immunosuppressive steroids and azathioprine were discontinued. Despite lowering immunosuppression, cardiac function slowly stabilized throughout the patient's hospital course. Left-sided MCS was removed on hospital day 28. LVEF improved to 25% off all circulatory support prior to discharge. High-sensitivity troponin T and CK-MB concentrations improved from the time of transfer to 41,143 ng/ml (normal values are 0 to 22 ng/ml) and 94 ng/ml (normal values 0.0 to 4.8 ng/ml), respectively, to 1,148 ng/ml and 4 ng/ml at 1 week after MCS was removed (**Figure 2**). Mycophenolate mofetil therapy was initiated after CMV titers decreased (990 copies/ml; white blood count: 9.8 1,000/mm^3). The patient was weaned from all circulatory support and discharged to a long-term acute care facility with cyclosporine, 75 mg twice daily, and mycophenolate mofetil, 500 mg twice daily. He was discharged on intermittent hemodialysis due to end-stage persistent anuric renal failure.

ABBREVIATIONS AND ACRONYMS

BNP = B-type natriuretic peptide

CMV = cytomegalovirus

EMB = endomyocardial biopsy

GCM = giant cell myocarditis

HF = heart failure

LVEF = left ventricular ejection fraction

TTE = transthoracic echocardiogram

DISCUSSION

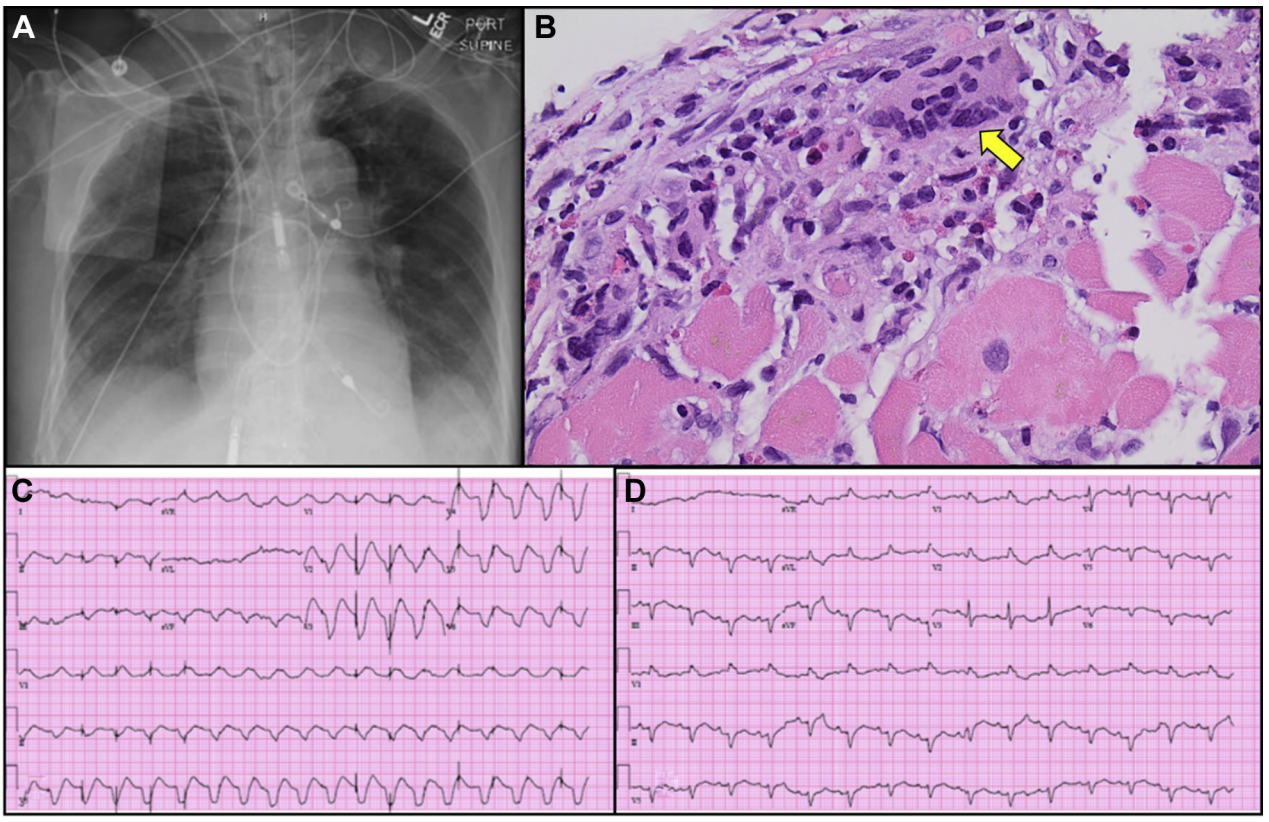
GCM is a rare cause of myocarditis, typically presenting as fulminant HF and/or episodes of ventricular arrhythmia (1,2). GCM primarily affects middle-aged adults of both sexes at a median age of 43 to 53 years at onset (1,3). The diagnosis requires histopathological evidence of giant cells on EMB, and treatment consists of hemodynamic support with vasopressors, inotropes, MCS, combined immunosuppression, and ultimately transplantation (3). The prognosis is extremely poor, with an international registry demonstrating that GCM carries a significantly worse prognosis than other forms of fulminant myocarditis (4). A French multicenter registry reported 100% mortality or transplantation in patients with GCM requiring MCS (5).

The present case is unique because the patient was much older than the average age of GCM patients (1).

TABLE 1 Clinical Variables upon Hospital Transfer After Left Ventricular Microaxial Blood Pump Placement on Dobutamine, Dopamine, and Norepinephrine

High-sensitivity troponin T (reference: 0 to 22 ng/ml), ng/ml	41,143
C-reactive protein (reference 0.0 to 0.5 mg/dl), mg/dl	7.9
Lactate (reference: 0.5 to 2.0 mmol/l), mmol/l	4.7
White blood cell count (reference: 4.0 to 10.0 1,000/mm^3), 1,000/mm^3	20.0
Eosinophils (0.0% to 6.0%), %	0
Cardiac output (Fick), l/min/m^2	3.39
Cardiac index (Fick), l/min/m^2	1.82
Ejection fraction (by transthoracic echocardiogram), %	12

FIGURE 1 Patient Chest Radiograph, Endomyocardial Biopsy, and Electrocardiograms



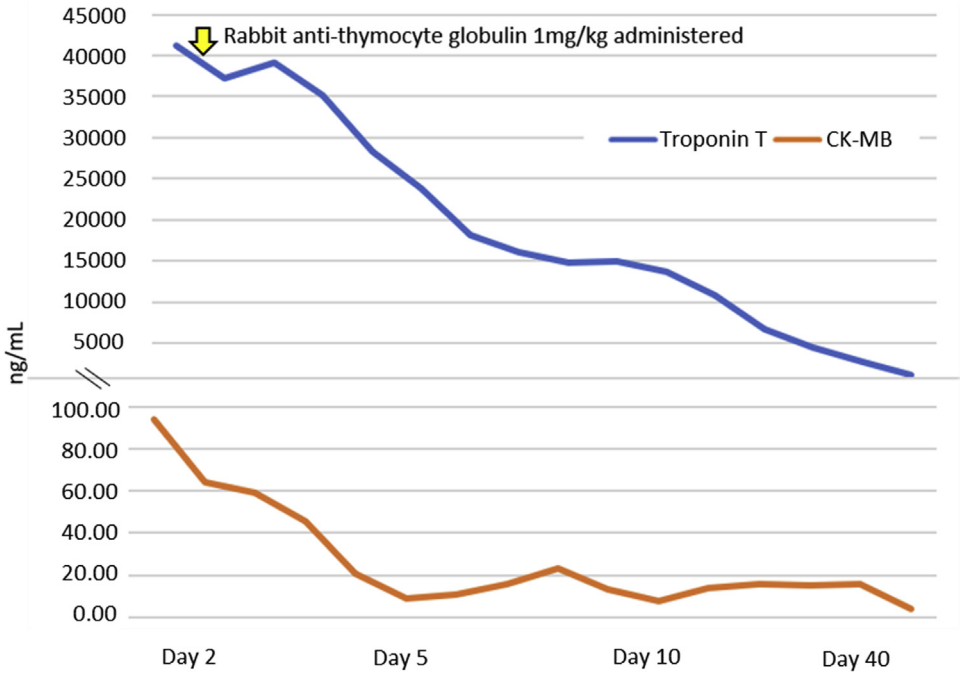
(A) Radiography shows biventricular microaxial blood pumps. **(B)** Hematoxylin-eosin stain of endomyocardial biopsy with giant cell **(yellow arrow)**. **(C)** Electrocardiogram shows ventricular tachycardia upon transfer. **(D)** Electrocardiogram showing recovery of sinus rhythm.

Although GCM is widely reported to affect middle-aged adults, the medical literature suggests that this is due to an underdiagnosis, with many patients being diagnosed at autopsy.

The patient's age and comorbidities provided a formidable challenge to his management, as they precluded both transplantation and durable MCS. Although a variety of temporary MCS devices are available, including intra-aortic balloon pump, temporary axial flow devices, and venous arterial-extracorporeal membrane oxygenation (VA-ECMO), this patient needed significant biventricular temporary support which limited his treatment options to axial flow devices or VA-ECMO. We chose biventricular temporary microaxial pumps for 2 reasons. First, they avoid the issue of increased afterload in VA-ECMO while providing percutaneous biventricular unloading (6). Second, the patient was already receiving left-sided intravascular microaxial blood pump, so it was easier to add right ventricular support instead of placing VA-ECMO. Although there was a favorable short-term outcome for this patient, it is worth noting that prolonged microaxial pump support may also be associated with a risk of complications. Other approaches to MCS in such settings would be reasonable to consider when accounting for patient- and center-specific factors.

Additionally, this patient also followed the suggested multiple-drug immunosuppressive regimen including antithymocyte globulins. Published case series have used different protocols. One study used rabbit antithymocyte globulin and pulse-dose steroids alone, whereas other studies recommended azathioprine, prednisone, and cyclosporine or alternatives such as mycophenolate mofetil or methotrexate (3,7). Given that this patient was not a candidate for transplantation due to his age, rabbit antithymocyte globulin, pulse-dose steroids, and cyclosporine were used as were a maintenance immunosuppressive regimen of cyclosporine, prednisone, and azathioprine. That regimen required a few weeks before a tangible improvement was obtained (12 days for the recovery of

FIGURE 2 Troponin T and CK-MB Trends During Hospitalization



CK-MB = creatine kinase-myocardial band.

the atrioventricular block and 28 days for the weaning from the MCS), which is consistent with previously described cases of GCM and other causes of myocarditis (2,6,8). One complication of this patient's high-dose immunosuppression, however, was the reactivation of CMV infection, requiring modification of his immunosuppressive regimen. In retrospect, the patient might have benefited from consideration of prophylactic antimicrobial therapy in conjunction with aggressive immunosuppression.

FOLLOW-UP

Two weeks later, the patient was readmitted to another hospital with septic shock. Vital signs upon admission showed a low-grade fever of 100.6°F, heart rate of 92 beats/min, and blood pressure of 92/64 mm Hg. Physical examination revealed dry mucous membranes and cold extremities without clinical signs of heart failure. His troponin-I concentration of 0.93 ng/ml (normal values are 0.0 to 0.03 ng/ml) suggested acute decompensated HF; however, bacteremia due to high-grade methicillin-resistant *Staphylococcus aureus* infection, likely from his dialysis catheter, and colitis from *Clostridium difficile* infection made overwhelming infection much more likely as the cause of decompensation. Despite broad-spectrum antibiotics and maximal vasopressor support, he died 93 days after his initial presentation.

This patient's sepsis was likely due to multiple factors, including his recent prolonged hospitalization, ongoing hemodialysis, and immunosuppression. However, his survival from discharge from the authors' hospital to 3 months illustrates the necessity of immunosuppression for a disease state for which the rate of mortality or heart transplantation has been shown to be 63% at 60 days from onset and 81% at 3 years of follow-up (3).

CONCLUSIONS

This paper describes a case of GCM in an elderly patient with partial recovery following combined immunosuppression and prolonged biventricular microaxial blood pump support. In conclusion, this report illustrates a feasible approach to treating elderly patients who otherwise could not undergo transplantation or receive durable MCS.

ADDRESS FOR CORRESPONDENCE: Dr. Eric Adler, Division of Cardiovascular Medicine, University of California San Diego, Sulpizio Cardiovascular Center, 9434 Medical Center Drive, La Jolla, California 92037. E-mail: eradler@health.ucsd.edu.

REFERENCES

1. Cooper L, Berry G, Shabetai R. Idiopathic giant-cell myocarditis–natural history and treatment. N Engl J Med 1997;336:1860–6.

2. Ammirati E, Oliva F, Belli O, et al. Giant cell myocarditis successfully treated with antithymocyte globuline and extracorporeal membrane oxygenation for 21 days. J Cardiovasc Med 2016;17 Suppl 2:e151–3.

3. Kandolin R, Lehtonen J, Salmenkivi K, et al. Diagnosis, treatment, and outcome of giant-cell myocarditis in the era of combined immunosuppression. Circ Heart Fail 2013;6:15–22.

4. Ammirati E, Veronese G, Brambatti M, et al. Fulminant versus acute nonfulminant myocarditis in patients with left ventricular systolic dysfunction. J Am Coll 2019;73:299–311.

5. Montero S, Aissaoui N, Tadie J, et al. Fulminant giant-cell myocarditis on mechanical circulatory support: management and outcomes of a French multicentre cohort. Int J Cardiol 2018;253:105–12.

6. Tschöppe C, Van Lithout S, Klein O, et al. Mechanical unloading by fulminant myocarditis: Lv-Impella, Ecmella, Bi-Pella, and Propella concepts. J Cardiovasc Transl Res 2019;12:116–23.

7. Suarez-Barrientos A, Wong J, Bell A, et al. Usefulness of rabbit anti-thymocyte globulin in patients with giant cell myocarditis. Am J Cardiol 2015;116:447–51.

8. Ammirati E, Cipriani M, Lilliu M, et al. Survival and left ventricular function changes in fulminant versus nonfulminant acute myocarditis. Circulation 2017;136:529–45.

KEY WORDS **acute heart failure, cardiac assist devices, hemodynamics, inotropes**