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MINI-FOCUS ISSUE: HEART FAILURE

ADVANCED

CASE REPORT: CLINICAL CASE

Use of TandemHeart as Bridge to Recovery for Antibody-Mediated Rejection in a Heart Transplant Patient

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ABSTRACT

Antibody-mediated rejection is a major cause of graft failure, mortality, and morbidity among cardiac transplant recipients. We present the first reported case of TandemHeart (LivaNova, Pittsburgh, Pennsylvania) used in the management of antibody-mediated rejection associated with cardiogenic shock. (**Level of Difficulty: Advanced.**) (J Am Coll Cardiol Case Rep 2020;2:2358–62) © 2020 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/).

A 57-year-old Black man presented to the hospital 5 years after orthotopic heart transplantation (OHT) with a week of dry cough, dyspnea, fatigue, abdominal pain, and lower extremity edema. He reported fever, chills, and symptoms of upper respiratory infection.

On presentation, he was afebrile, with blood pressure of 84/62 mm Hg, a heart rate of 111 beats/min, a respiratory rate 22 breaths/min, and oxygen saturation of 99% on 2 liters by nasal cannula. On physical examination, he appeared in distress. The jugular venous pressure was elevated at 14 cm H_2O. Cardiac examination showed tachycardia with a regular rhythm, normal S_1 and S_2, with no murmurs. Bibasilar crackles were present on lung auscultation. His liver span was increased at 16 cm. Peripheral pulses were symmetrical, and he had bilateral lower extremity edema.

LEARNING OBJECTIVES

- To recognize AMR when a heart transplant recipient presents with signs of graft dysfunction.
- To understand the role of MCS in AMR.

PAST MEDICAL HISTORY

He had a history of ischemic cardiomyopathy after HeartMate II left ventricular assist device placement, followed by OHT 2 years later. His post-transplant course was uncomplicated. He had no major infections, rejection episodes, or angiographic evidence of coronary allograft vasculopathy (performed 1 year before his presentation). No donor-specific antibodies were noted before admission. His immunosuppression regimen included tacrolimus (goal of 5 to 8 ng/ml) and mycophenolic acid, 1000 mg twice a day. Prednisone was weaned 2 years after his transplant procedure. No recent medication changes had been made.

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DIFFERENTIAL DIAGNOSIS

The initial differential diagnosis included acute rejection with allograft failure, septic shock, and cardiac allograft vasculopathy.

INVESTIGATIONS

Laboratory testing revealed a creatinine level of 3.3 mg/dl (baseline 1.4 mg/dl), a B-type natriuretic peptide value of 4,900 pg/ml, and a bicarbonate level of 13 mg/dl. His tacrolimus level on admission was 5.9 ng/ml. The electrocardiogram revealed sinus tachycardia with low voltage and right-axis deviation (**Figure 1**). Chest radiography revealed pulmonary vascular congestion and mild cardiomegaly (**Figure 2**). The echocardiogram showed global hypokinesis with a left ventricular ejection fraction (LVEF) of <20% (previous LVEF >55%). Right-sided heart catheterization showed a right atrial pressure of 15 mm Hg, pulmonary artery pressure of 40/25 mm Hg (mean of 30 mm Hg), cardiac output by Fick method of 3.46 l/min, cardiac index of 1.6 l/min/m^2, and a pulmonary capillary wedge pressure of 23 mm Hg. Endomyocardial biopsy findings were consistent with acute cellular and antibody-mediated rejection (AMR) (International Society for Heart and Lung Transplantation grade 1, pathological antibody-mediated rejection [pAMR] grade 2+ (**Figures 3A to 3D**).

MANAGEMENT

Given the high suspicion of severe rejection on admission, the patient was empirically started on pulse-dose intravenous steroids. After the biopsy results came back, the following regimen was added: antithymocyte globulin, intravenous immunoglobulin, rituximab, and bortezomib. He also underwent plasmapheresis for 5 days (**Table 1**). His home dose of mycophenolate mofetil and tacrolimus were continued.

He was also started on dobutamine (5 μg/kg/min) and epinephrine (0.04 μg/kg/min). Given his persistent hypoperfusion, as evidenced by lactic acidosis and anuria, the following morning an intra-aortic balloon pump (IABP) was placed, and sustained low-efficiency dialysis was initiated.

His hemodynamic status and urine output improved. However, on hospital day 5, telemetry showed atrial fibrillation with a rapid ventricular rate along with runs of nonsustained ventricular tachycardia. His central venous pressure was 18 mm Hg, his blood pressure dropped to 90/60 mm Hg, and his urine output decreased to 15 ml/h. Laboratory values showed worsening renal function and lactic acidosis. Attempts to increase epinephrine and dobutamine were limited by his arrhythmia. He was loaded with amiodarone, followed by a continuous infusion. Given his hemodynamic instability despite current support, he underwent successful synchronized cardioversion and was taken to the cardiac catheterization laboratory for TandemHeart (LivaNova, Pittsburgh, Pennsylvania) placement. He initially required 3.2 l/min of cardiac output support. Arterial line pulsatility was lost because he was entirely dependent on the device. He maintained sinus rhythm, and urine output increased to 3 to 6 l/day.

The patient was continued on the rejection medication regimen described in **Table 1**. He was slowly weaned from circulatory support with the TandemHeart; and by day 15 the TandemHeart was removed and replaced with an IABP. All circulatory support was removed on hospital day 21. A repeat echocardiogram showed improvement of the LVEF to 55%.

DISCUSSION

To our knowledge, this case represents the first report of TandemHeart as a successful bridge to recovery from cardiogenic shock (CS) secondary to acute AMR in OHT. AMR remains an important problem for clinical management of patients who have undergone OHT because of the complexity of the diagnosis and the paucity of evidence supporting current therapies.

Treatment of AMR is based on 2 general principles: interruption of the immune-mediated cardiac injury

ABBREVIATIONS AND ACRONYMS

AMR = antibody-mediated rejection

CS = cardiogenic shock

ECMO = extracorporeal membrane oxygenation

IABP = intra-aortic balloon pump

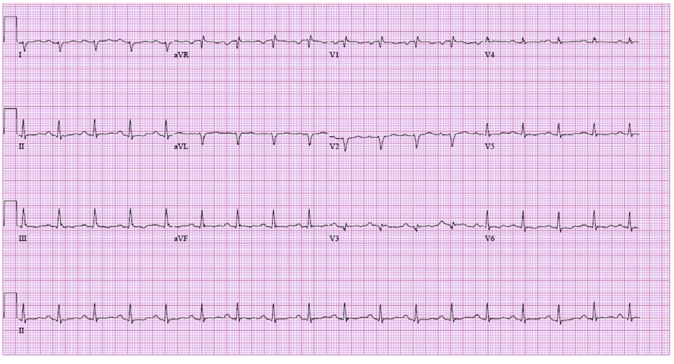
LVEF = left ventricular ejection fraction

MCS = mechanical circulatory support

OHT = orthotopic heart transplantation

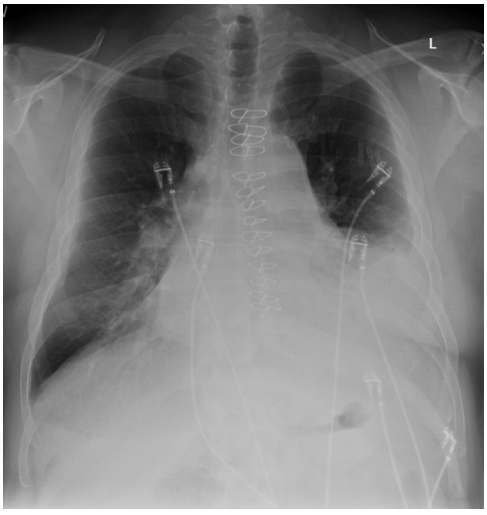
pAMR = pathological antibody-mediated rejection

FIGURE 1 Electrocardiogram



Electrocardiogram showing sinus tachycardia with low-voltage and right-axis deviation.

FIGURE 2 Chest Radiograph



The anteroposterior view shows bilateral pulmonary vascular congestion and mild cardiomegaly. L = left.

and supportive care for graft dysfunction. Halting the immune response can be achieved by removing circulating antibodies, reducing production of additional antibodies, and decreasing cellular response (1). No large randomized trials are available to guide therapy, and generally, recommendations are based on expert consensus many times by extrapolating studies from other solid organ transplantation experiences, primarily kidney. Differences in protocols to treat rejection among centers represent a reality. However, most physicians would treat a patient with suspected pAMR 0 with donor-specific antibodies or confirmed AMR (pAMR grade 1 to 3) in the setting of graft dysfunction. The usual treatment for AMR includes steroids, intravenous immunoglobulin, plasmapheresis, rituximab, and thymoglobulin. Refractory cases are treated with newer and more aggressive agents, such as alemtuzumab, bortezomib, or eculizumab (1).

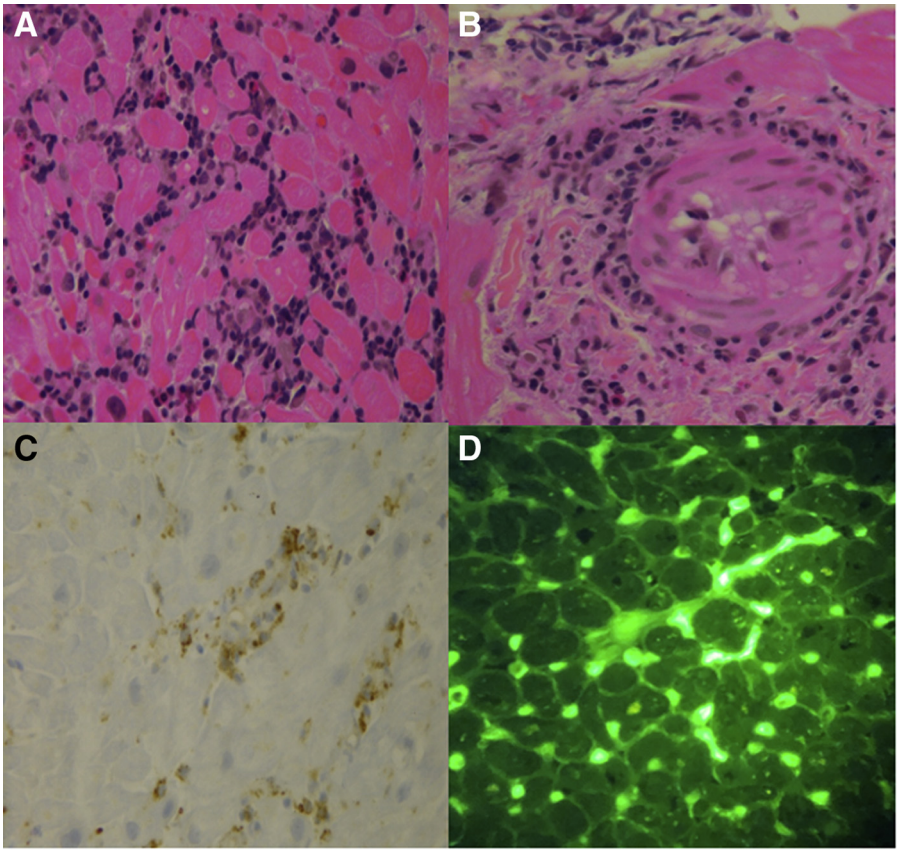
CS is the most severe form of allograft dysfunction. The prevalence of CS in the setting of AMR is 30% to 47%; and its prognosis is poor despite aggressive immunosuppressive therapies (2,3). The use of temporary mechanical circulatory support (MCS) in OHT recipients because of early or late complications has been reported. Most of the published evidence is linked to the use of extracorporeal membrane oxygenation (ECMO) (4–6). Kittleson et al. (7) identified adult patients who underwent OHT with CS requiring ECMO support. ECMO was used for 37 episodes of CS in 32 post-OHT patients. ECMO support included pre-emptive therapy, defined as therapy in patients with escalating inotropic requirements despite IABP support, and salvage therapy, defined as therapy in patients in cardiac arrest who were undergoing cardiopulmonary resuscitation with chest compressions. Of 24 biopsies performed, only 6 cases had evidence of AMR. The evidence supporting the use of other forms of temporary MCS is even more limited. Beyer et al. (8) reported a case of CS secondary to AMR requiring MCS while the patient was undergoing intense immunosuppression. This patient underwent implantation of an intravascular microaxial blood pump (Impella 2.5, Abiomed, Danvers, Massachusetts) device as a successful bridge to recovery (8).

In our patient, IABP and increasing inotropic requirements did not provide sufficient support, as demonstrated by persistent lactic acidosis and renal dysfunction requiring renal replacement therapy. At that time, the decision was made to upgrade to another temporary MCS device for hemodynamic stabilization. A collaborative heart team assessed his candidacy for percutaneous ventricular assist devices, including Impella or TandemHeart. In this case, the decision not to use the Impella device was based on the presence of frequent ventricular ectopy and the patient's clinical instability to undergo surgical implantation of an Impella 5.0 device. TandemHeart significantly reduces pre-load and augments cardiac output, with the ability to pump up to 5 l/min of cardiac support. After atrial septal puncture, the 21-F inflow cannula is inserted percutaneously through the common femoral vein and is advanced across the interatrial septum into the left atrium over an 0.025-inch guidewire (Toray Industries, Tokyo, Japan). The pump propels blood by means of a magnetically driven 6-bladed impeller through the outflow port and returns it to the aorta through a 17-F cannula inserted through the common femoral artery (9).

FOLLOW-UP

After a prolonged hospital course (31 days), the patient was transferred to an inpatient rehabilitation facility. Repeat endomyocardial biopsy and right-sided heart catheterization 11 weeks after his initial presentation showed improved albeit persistent AMR graded pAMR 1(I+) and an increased cardiac index of 3.98 l/min/m^2. He was clinically asymptomatic and doing well. Therefore, no changes were made to his immunosuppressive regimen.

FIGURE 3 Histopathological and Immunopathological Biopsy Features of Antibody-Mediated Rejection



(A and B) Biopsy sample stained with hematoxylin and eosin shows that the cellular infiltrates are within vessels and include polymorphonuclear leukocytes. Endothelial cell swelling is present. **(C and D)** Immunoperoxidase and immunofluorescence stains show diffuse moderate C4d deposition in capillaries.

TABLE 1 Timeline of Treatment and Interventions During Hospital Course

Hospital Day	Treatment and Intervention
1	1.25 g of methylprednisolone
2	1 g of methylprednisolone, plasmapheresis, antithymocyte globulin, endomyocardial biopsy, IABP placement
3	1 g of methylprednisolone, antithymocyte globulin, plasmapheresis
4	1 g of methylprednisolone, antithymocyte globulin, plasmapheresis
5	10 mg maintenance of prednisone (which continues through discharge), antithymocyte globulin, plasmapheresis, TandemHeart placement
6	Antithymocyte globulin, plasmapheresis
8	IVIG 1 g/kg
11	Bortezomib
14	Bortezomib
15	Rituximab 1 g intravenously, TandemHeart removed, IABP placed
21	IABP removed
22	Bortezomib
30 (outpatient)	Rituximab
38 (outpatient)	IVIG 1 g/kg

IABP = intra-aortic balloon pump; IVIG = intravenous immunoglobulin.

CONCLUSIONS

Early initiation of MCS should be considered in patients with AMR associated with graft dysfunction and hemodynamic instability. Selection of an MCS device should be individualized according to the patient's clinical presentation and institutional experience.

AUTHOR DISCLOSURES

Dr. Desai is a consultant and speaker for Abbott. Dr. Rajan Patel is a speaker for LivaNova and Boston Scientific; and is on the advisory board of Abiomed. Selim Krim is a consultant for Abbott and CareDx. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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