JACC: CASE REPORTS VOL. 3, NO. 7, 2021

CASE REPORT

INTERMEDIATE

CLINICAL CASE: EDITOR'S HIGHLIGHTS

A Case for Re-Gifting

Amanda C. Coniglio, MD,[a] Richa Agarwal, MD,[a] Jacob N. Schroder, MD,[b] Robert J. Mentz, MD,[a,c] Carmelo A. Milano, MD,[b] Adam D. DeVore, MD, MHS,[a,c] Chetan B. Patel, MD[a]

ABSTRACT

Many patients die while waiting for a heart transplant. Therefore, it is vital that all suitable organs are used for transplantation. We present a case of an allograft that was transplanted twice and outline considerations regarding tissue typing, the impact of repeated ischemic time, and ethical considerations with allograft retransplantation. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2021;3:1010–2) © 2021 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/).

INTRODUCTION

Heart transplantation (HT) offers a lifesaving therapeutic option for >3,000 patients per year who have advanced heart failure. Unfortunately, HT remains a finite resource. A shortage of suitable organs within a specified geographic radius, strict recipient acceptance criteria, and immunologic matching limitations can leave thousands of patients with prolonged wait times and risk of deterioration. In rare circumstances, a transplant recipient may have a fatal complication. If the allograft is functioning well, it is possible to consider retransplantation of the heart. To date, there are <10 published case reports of cardiac allograft retransplantation to a second recipient (1–7). Although previous reports highlighted the feasibility of heart retransplantation, we present a novel case of retransplantation within 10 days of the initial HT into a highly allosensitized recipient.

LEARNING OBJECTIVES

- To understand the feasibility and risk-to-benefit ratio of early retransplantation of a cardiac allograft.
- To be able to evaluate the immunologic risk of retransplantation to ensure compatibility.

HISTORY OF PRESENTATION, INVESTIGATIONS, AND MANAGEMENT

A 65-year-old woman with anthracycline-induced cardiomyopathy presented with cardiogenic shock. She was stabilized with an intra-aortic balloon pump and inotropic support and was listed for HT. She did not have pre-formed anti-human leukocyte antigen (HLA) antibodies. A suitable organ was accepted and transported to our center by traditional cold static storage. The HT was performed through a primary sternotomy without complication, and there was no evidence of primary graft dysfunction. Total ischemic time was 260 min, and the T- and B-cell crossmatch results were negative. The recipient received induction therapy with basiliximab and was started on standard immunosuppression with tacrolimus, mycophenolate, and prednisone. The patient was extubated and transferred to a stepdown floor within 5 days. Unfortunately, she had a spontaneous

From the [a]Department of Medicine, Duke University School of Medicine, Durham, North Carolina, USA; [b]Department of Surgery, Duke University School of Medicine, Durham, North Carolina, USA; and the [c]Duke Clinical Research Institute, Duke University School of Medicine, Durham, North Carolina, USA.

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 Author Center.

Manuscript received January 11, 2021; revised manuscript received March 12, 2021, accepted March 25, 2021.

ISSN 2666-0849 https://doi.org/10.1016/j.jaccas.2021.03.025

hemorrhagic stroke on post-operative day 8 and was pronounced brain dead. She continued to have normal cardiac, liver, and renal function, and her family consented for organ donation including the recently transplanted heart.

A 30-year-old man with a history of congenital heart disease (repaired ventricular septal defect, subaortic membrane resection with aortic root and valve replacement with a homograft) who now had non-ischemic cardiomyopathy was active on the HT transplant waitlist at our institution (Duke University Medical Center, Durham, North Carolina). In the original match run for this donor heart, this patient was considered, but the organ was not accepted for him given the higher-priority status of the first recipient.

He had a number of pre-formed anti-HLA antibodies as a result of previous surgical procedures and transfusions. On thorough assessment, he had 2 antibodies in common with the original donor HLA phenotype (mean fluorescence intensity [MFI] 3,326 and 2,448) and 1 antibody in common with the second donor (MFI 5,513). The concentration of the antibodies against the first donor and subsequently the heart tissue was at a level that would be acceptable in our program.

When the patient was notified of the offer, he was informed of the unique situation of repeat transplantation and accepted the possible increased associated risk. He underwent HT through a redo sternotomy with a total ischemic time of 98 min. His previous homograft was removed, but part of the aorta from the first recipient was used for anastomosis. There was no evidence of primary graft dysfunction. T- and B-cell crossmatch results were both positive, so he received induction therapy with rabbit antithymocyte globulin (4 doses) and plasmapheresis (5 sessions), followed by standard immunosuppression with tacrolimus, mycophenolate, and prednisone. His post-operative course was complicated by moderate right ventricular dysfunction requiring inotropic support for 6 days. Right-sided heart catheterization on post-operative day 8 off of support showed normal filling pressures and a cardiac index of 2.4 L/min/m^2. Routine post-transplant cardiac magnetic resonance showed normal biventricular function without wall motion abnormalities. There was a small focus of late gadolinium hyperenhancement in the mid-left ventricular inferior wall that was believed to be related to reperfusion injury or an embolic origin (**Figure 1**). He was discharged from the hospital 12 days after HT. He has continued to do well post-transplant without complications at 9 months of follow-up and no evidence of significant cellular or antibody-mediated rejection.

DISCUSSION

Although this report and those previously reported outline successful retransplantation of cardiac allografts, we chose to highlight key considerations that may influence outcomes.

ABBREVIATIONS AND ACRONYMS

HLA = human leukocyte antigen

HT = heart transplantation

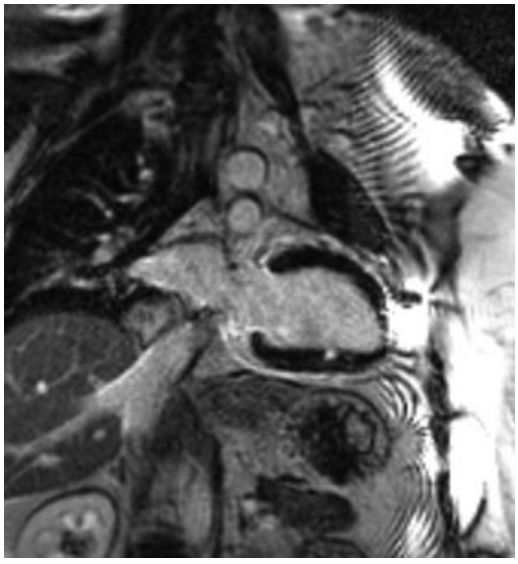
MFI = mean fluorescence intensity

TECHNICAL ASPECTS. There is an unquantifiable risk of insult to any organ in a brain-dead individual waiting for transplantation because of physiological (catecholamine surge) and electrolyte derangements. This is a risk for all transplanted organs, but the risk of repeated insults in a retransplanted allograft could result in compounded harm. This is of particular concern in this case, when retransplantation occurred shortly after the original HT when the organ was likely still recovering from the initial insult with a risk of ongoing cellular edema. In this case, cardiac magnetic resonance demonstrated preserved cardiac function and minimal evidence of hyperenhancement (thought to represent reperfusion injury) despite repeated ischemic insults. This case highlights the feasibility and safety of retransplantation of an allograft with a short chronological delay.

From a surgical standpoint, retransplantation within months or years of the initial HT poses a risk of scar tissue or adhesion on chest re-entry making retransplantation more difficult. In this case, the organ was procured within 2 weeks after initial HT, and there were no significant adhesions. It is also important to minimize tissue from the first recipient when transplanting the organ into the second recipient to avoid increased immunologic risk. Unfortunately, this was not possible in our case because of the need for aortic tissue to replace the second recipient's previous homograft. Although a polyethylene terephthalate (Dacron, INVISTA, Kennesaw, Georgia) graft was considered, this was believed to pose a higher risk because of the presence of prosthetic material. Even though the approach used may increase immunologic risk, this case highlights successful transplantation of tissue from both donors with enhanced upfront immunosuppression and management.

TISSUE TYPING CONSIDERATIONS. Retransplantation of an allograft raises concerns regarding exposure to immune complexes from multiple individuals. In this case, the second recipient had known pre-formed antibodies to both the original heart donor and the second recipient, thus leading to an anticipated positive crossmatch. Although the antibody against an HLA antigen from the first recipient was at an MFI that would otherwise preclude consideration of organ acceptance (>5,000 MFI), minimal tissue transfer

FIGURE 1 Late Gadolinium Hyperenhancement of the Mid-Left Ventricular Inferior Wall Representing Approximately 1% of the Overall Myocardial Mass



from the first to second recipient was anticipated. Discussions should be conducted with the transplant team, the pathology team, and the HT recipient before acceptance of organs with anticipated positive crossmatch, with consideration for longer-term surveillance for rejection to optimize the longevity of the cardiac allograft.

ETHICAL CONCERNS. Retransplantation may create ethical dilemmas for the multiple parties involved. In this case, the first HT and retransplantation both occurred at the same institution with the same transplant team. It may be taxing to serve as both the team caring for the initial transplant recipient and their family while also weighing the benefits of retransplantation to another patient. It is also difficult to discuss organ donation with the first recipient's family because they struggle with the mixed emotions associated with watching end-stage heart failure, HT, and then a tragic loss all within a 2-week period. The role of being a steward of the transplanted organ affords the opportunity for continued altruism through organ donation and may ease the grieving process for families.

As previously outlined, there remain theoretical increased risks of adverse events with retransplantation that are unable to be fully quantified. We believe that this issue should be discussed with the potential second recipient before acceptance of the organ.

CONCLUSIONS

Retransplantation may be associated with an increased risk of adverse events, but thus far, cardiac allograft retransplantation has been successful in the case outlined here. There remain unique immunologic and ethical considerations that should be discussed with the multidisciplinary transplant team and organ recipient. Organ retransplantation remains a rare event but should be considered under appropriate circumstances, to re-gift all available organs.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

Dr. Mentz has received research support and honoraria from Abbott, American Regent, Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Boston Scientific, Cytokinetics, Medtronic, Merck, Novartis, Roche, Sanofi, and Vifor. Dr. DeVore has received research support from the American Heart Association, Amgen, AstraZeneca, Bayer, Intra-Cellular Therapies, American Regent, Inc, the National Heart, Lung and Blood Institute, Novartis, and the Patient-Centered Outcomes Research Institute; and also provides consulting services for Amgen, AstraZeneca, Bayer, CareDx, InnaMed, LivaNova, Mardil Medical, Novartis, Procyrion, scPharmaceuticals, Story Health, and Zoll. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr. Dr. Chetan B. Patel, Duke University School of Medicine, DUMC 3034, Durham, North Carolina 27710, USA. E-mail: chetan.patel@duke.edu.

REFERENCES

1. Nemec P, Bedanova H, Ostrizek T. Successful reuse of the transplanted heart. Ann Thorac Surg 2010;90:1337–8.

2. Meiser BM, Uberfuhr P, Reichenspurner H, et al. One heart transplanted successfully twice. J Heart Lung Transplant 1994;13:339–40.

3. Simsir SA, Fontana GP, Czer LS, Schwarz ER. Heart allograft transplanted twice. Eur J Cardiothorac Surg 2008;34:918–9.

4. Planinc M, Mihaljevic T, Jarrett CM, et al. One heart in 3 patients. Ann Thorac Surg 2012;94:e143–4.

5. Mullen JC, Kuurstra EJ, Burhani MS, et al. Successful recycling of a previously transplanted heart: another option for limited resources. Can J Cardiol 2014;30:1460.e1–2.

6. Pasic M, Gallino A, Carrel T, et al. Brief report: reuse of a transplanted heart. N Engl J Med 1993;328:319–20.

7. Rodriguez-Gonzalez E, Hernandez-Perez FJ, Gomez-Bueno M, et al. One heart for two recipients: an effective option to increase donor organ availability in heart transplantation. Rev Esp Cardiol (Engl Ed) 2016;69:1220–1.

KEY WORDS cardiac transplant, imaging, systolic heart failure