Donor transmitted anterior myocardial ischaemia in a teenager: how to proceed?

Laszlo Göbölös, Maurice Hogan, Mosaad El-Banna, Feras Bader, Emin Murat Tuzcu & Gopal Bhatnagar

Emirates Med J 2021; 2(2): 146-150
CASE REPORT

Donor-transmitted Anterior Myocardial Ischaemia in a Teenager: How to Proceed?

Laszlo Göbölös, Maurice Hogan, Mosaad El-Banna, Feras Bader, Emin Murat Tuzcu and Gopal Bhatnagar

1 Department of Cardiac Surgery, Heart and Vascular Institute, Cleveland Clinic Abu Dhabi, Abu Dhabi, UAE
2 Department of Cardiac Anesthesia and Intensive Care, Cleveland Clinic Abu Dhabi, Abu Dhabi, UAE
3 Department of Cardiology, Heart and Vascular Institute, Cleveland Clinic Abu Dhabi, Abu Dhabi, UAE

Abstract:
Background: Heart transplantation remains the treatment of choice for end-stage heart failure patients, owing to the associated dual improvements in quality of life, and prognosis. The discrepancy between higher demand and supply of donor organs is the limiting factor, and is established universally. Increasing consideration of donor populations up to 65 years of age and marginal donor hearts has helped to facilitate the availability of potential grafts. However, grafts from older donors carry the mid-term increased risk of coronary allograft vasculopathy, including donor-transmitted coronary disease.

Case report: A 15-year-old female underwent orthotopic heart transplantation for non-ischaemic cardiomyopathy, the donor was a 44-year-old male. The recipient developed anterior wall ischaemia within a year requiring coronary angioplasty and stent implantation to treat the severe obstruction in the left anterior descending coronary artery. However, two months later, the patient was readmitted with in-stent restenosis. Therefore, to optimally revascularise the left anterior descending coronary artery, and minimise risks associated with re-sternotomy, a minimally invasive direct coronary artery bypass grafting of the left internal mammary artery to the left anterior descending artery was performed.

Conclusion: Surgical revascularisation in generalised coronary allograft vasculopathy is an inadequate option; repeat heart transplantation is the treatment of choice, albeit given its morbidity, should be reserved for a highly selected patient population. In localised coronary lesions, conventional coronary bypass surgery may be a feasible choice in selected patients with left anterior descending artery lesions. Minimal invasive techniques, such as minimally invasive direct coronary artery bypass grafting rather than robotic techniques, would be preferable for ease of approach and to limit the surgical re-do trauma.

Keywords: Heart transplantation, Donor transmitted coronary disease, Surgical revascularisation, Minimally invasive, MIDCAB, Myocardial Ischaemia.

1. INTRODUCTION

Heart transplantation (HTx) is the treatment of choice for improving both quality of life and prognosis of patients with advanced heart failure [1]. The discrepancy of increasing transplant candidates and available donor organs is a well-known phenomenon worldwide [2]. Most transplants nowadays result from multiple organ retrieval beating-heart brain-dead donors. Nevertheless, brain death is often associated with prominent physiological instability, that may lead to deteriora-
Donor transmitted coronary disease. Older donors also have higher rates of hypertension, dyslipidemia and smoking, according to recent studies. Therefore, a careful selection of both donors and recipients and close monitoring of CAV is suggested by Roig et al. [3]. Additional challenge in older donor screening arising from that families usually disagree to perform pre-donation coronary angiography (CAG), procurement district hospitals have no availability of CAG, or local caregiver physicians have no experience in undertaking CAG, and also concerned about the donor haemodynamics, and preservation of other organs’ function, specifically the kidneys [4]. Despite increasing consensus over donor management directions, several elements of these therapeutic pathways have not yet been subjected to controlled evaluation [2]. Due to a rising number of marginal donor hearts, it is widely accepted to investigate the coronary status of middle-aged donors either by conventional coronary angiography or computed tomographic angiography. However, current professional guidelines do not incorporate these criteria of donor assessment yet.

2. CASE REPORT

2.1. History of Presentation and Past Medical History

A 15-year-old female with a history of chronic non-ischemic cardiomyopathy underwent successful orthotopic heart transplantation in another medical institution. There was no further significant disease present in her past medical history. She was overweight preoperatively due to physical inactivity that has improved after the surgical procedures. The donor was a 44-year-old male with no known significant past medical history, and coronary imaging was not performed before organ harvest.

The transplant procedure was uneventful, with a cold ischemic time of less than 3 hours. There was no clinical evidence of early rejection, and the patient had an uneventful postoperative course. After transplantation, the patient was started on statin treatment (atorvastatin 80 mg OD) to help reduce the risk of CAV and was on dual immunosuppression therapy with tacrolimus (3 mg BD) and mycophenolate-mofetil (2000 mg BD).

2.2. Investigations

Post-transplant angiography at two months demonstrated a significant stenosis in the proximal left anterior descendent (LAD) involving the ostium, and circumflex (Cx) coronary arteries, the patient was treated by implantation of drug-eluting stents (DES) in both coronaries (LAD – Xience Sierra® 2.5x23 mm; Cx - Xience Sierra® 2.5x12 mm stent, Abbott, USA). Intravascular ultrasound investigation is applied as an institutional standard for all intravascular procedures as a diagnostic and quality control method. In this case, it was also essential to confirm the localised nature of the calcified coronary lesions. The right coronary showed no stenotic disease, and the coronary circulation was right dominant.

A further six months later, follow-up angiogram showed diffuse distal left main (LM) disease and total occlusion of the Cx. She underwent an uncomplicated percutaneous coronary intervention (PCI) with DES placement in the LAD and distal LM (LAD – Xience Sierra® 3.0x15 mm; LM - Xience Sierra® 3.5x15 mm stent, Abbott, USA). The Cx occlusion was not passable for the guidewire, but the distal vessel was retrogradely filled from the dominant right coronary via heterocoronary collaterals. A dobutamine stress echocardiography revealed no ischemia in the latter myocardial region.

Coronary angiogram one year after transplant demonstrated patent stents in the LM and LAD without disease progression in these vessels. The next angiogram five months later revealed in-stent-restenosis in the LAD (Fig. 1), a diagnosis which was also reinforced by a coronary computed tomographic angiogram (CTA) (Fig. 2). The 64-slice multidetector electrocardiography gated CTA demonstrated no diffuse coronary disease referring to a transplant vasculopathy.

Fig. (1). Coronal plane coronary angiography reveals significant proximal LAD stenosis.

Fig. (2). Heavily calcified in-stent restenosis of the LAD on coronary computed tomographic angiography (arrow indicates the lesion).

On all coronary angiographic encounters, myocardial biopsy samples were obtained showing no acute cellular rejection (ISHLT 2004 Grade 0R), and no histopathology findings of antibody-mediated rejection were present.
After the initial PCI, the patient was started on dual antiplatelet therapy.

2.3. Management

As the patient demonstrated rapid disease progression in the LAD stent despite adequate immunosuppression and statin therapy, surgical revascularisation was recommended.

Eighteen months after her HTx, we performed a left internal mammary (LIMA) to LAD minimal invasive direct coronary artery bypass grafting (MIDCAB) via a 6 cm parasternal incision in the 4th intercostal space. The graft showed an excellent quality on Doppler flowmetry intraoperatively, and following an uneventful postoperative course, the patient was discharged on the fifth postoperative day.

2.4. Follow-up

At outpatient follow-up after six months postoperatively, the patient reported no symptoms and good exercise tolerance, echocardiography showed normal biventricular function, dobutamine stress echocardiography demonstrated no ischemic burden. A CAG performed on this patient encounter revealed a patent LIMA graft with excellent peripheral outflow (Fig. 3).

![Fig. (3). Six months CAG follow-up demonstrates patent LIMA to LAD graft.](Image)

Yearly follow-up angiographic investigations showed patent LIMA graft and no further progress of the coronary disease; stress echocardiography revealed no ischemic myocardial territories.

The patient has a stable condition after two years on acetylsalicylic-acid (100 mg OD), atorvastatin (80 mg OD), tacroliimus (1.5 mg BD) and mycophenolate-sodium (720 mg BD).

3. DISCUSSION

Post-transplant CAV poses a major challenge in the ongoing management of heart recipients, especially younger patients. CAV is responsible for more than a quarter of late mortality in children after HTx and has multifactorial aetiology, but donor age is a significant factor in the development of coronary lesions [4, 5]. If there is a pre-existing coronary artery disease of the donor present, the atherosclerotic progression is accelerated by the factors which generally contribute to CAV. As a result of graft denervation, CAV does not lead to early anginal symptoms, and CAG remains the method of early disease detection [6] with 5% incidence in year one, 15% in year five, and 30% ten years after HTx. A maximal intimal thickness of ≥0.5 mm on initial IVUS also has a predictive value of donor transmitted coronary disease [5]. Recent imaging researchers suggest that computed tomographic angiography (CTA) facilitated quantitative coronary wall assessment may have a role in early non-invasive detection of CAV; 74% of coronary lesions were detectable at baseline CTA read, and 80% of lesions were diagnosed on follow-up investigations. Coronary CTA combines the advantages of IVUS and CAG as able to assess both coronary wall and lumen features [7]. Donor hearts with moderate coronary artery disease do not affect survival, freedom from cardiac-related adverse events in adult recipients, but routine use of CAG in donor selection appears justified [8]. If the recipient shows signs of established ischemia resulting from donor transmitted coronary disease, the ischaemic burden has to be eliminated to avoid adverse outcomes. Donor grafts with the single-vessel coronary disease might be accepted as marginal hearts; however, concomitant revascularisation at the transplantation should be considered. Grafts having double- or even triple-vessel coronary disease carry a high risk for early graft failure. Time from the transplant has an essential impact on the established coronary atherosclerosis, probably resulting from settling of host versus graft immune response. Beyond the first post-transplant year, the outcome of healthy grafts and grafts with donor-transmitted coronary atherosclerosis are comparable [9].

Medical management of CAV, just as for transmitted coronary disease should include statin, vasodilator and tailored immunosuppressive therapy to decrease allograft rejection and slowing down CAV progression, whilst minimising side effects. For cases poorly responsive to pharmacotherapy, and especially isolated lesions, percutaneous coronary intervention may be indicated. However, PCI offers a less favourable long-term outcome in donor-transmitted coronary disease [10].

Surgical revascularisation in generalised CAV is an inadequate option; repeat HTx is the treatment of choice [11]. In localised coronary lesions, conventional coronary bypass surgery may be a feasible choice in selected patients, particularly for LAD lesions. Patients post revascularisation require rigorous follow-up due to the potential for accelerated progression of coronary disease in transplanted hearts [11]. Applying a conventional surgical approach, re-do sternotomy commences with extensive adhesiolysis, that carries a high risk for infections, including fatal mediastinitis and poor wound healing in immunosuppressed. Minimal invasive techniques, such as the MIDCAB, rather than robotic techniques, may be preferable for ease of approach and limit surgical re-operative trauma. Our technical approach allowed accessing the LAD through a mini-thoracotomy, where the sternum was kept intact, and revascularisation was completed without an increased risk for wound infections or dehiscence. This procedure has provided satisfactory long-term results for a limited critical coronary lesion in an adolescent, delaying the necessity for an early retransplantation.
CONCLUSION

Heart transplantation stays the treatment of choice for end-stage heart failure patients, owing to the associated dual improvements in quality of life, and prognosis. The discrepancy between higher demand and supply of donor organs is the limiting factor, and is established universally. Increasing consideration of donor populations up to 65 years of age and marginal donor organs have helped to improve the availability of potential grafts. However, hearts from older donors carry the mid-term increased risk of coronary allograft vasculopathy, including donor transmitted coronary disease. In the detection of donor transmitted coronary disease, regular CAG follow-up is vital, and invasive procedures, including redo surgery, might be necessary to correct arterial lesions.

Learning Objectives

- The discrepancy between increasing demand and supply of donor organs is the limiting factor in heart transplantation.
- Marginal donor hearts have helped to increase the availability of potential grafts.
- Grafts from older donors carry the mid-term increased risk of coronary allograft vasculopathy and transfer of acquired coronary lesions.
- Donor coronary angiography or at least cardiac computed tomographic angiography is essential to avoid the transfer of acquired coronary lesions at heart transplantation.
- In the case of transferred coronary disease, if coronary angioplasty fails to correct the donor transmitted vascular lesions, a surgical procedure, if possible a minimally invasive should be considered.
- Long-term follow-up is mandatory in these patients.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

HUMAN AND ANIMAL RIGHTS

Not applicable.

CONSENT FOR PUBLICATION

Consent was obtained by patient's father.

STANDARDS OF REPORTING

CARE guidelines have been followed in this case report.

FUNDING

None.

CONFlict of interest

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Declared none.

REFERENCES

[1] Yancy CW, Jessup M, Bozkurt B, et al. 2017 ACC/AHA/HFSA Focused update of the 2013 ACCF/AHA guideline for the management of heart failure: A report of the american college of cardiology/american heart association task force on clinical practice guidelines and the heart failure society of america. J Am Coll Cardiol 2017; 70(6): 776-803.

[2] McKeown DW, Bonser RS, Kellum JA. Management of the heartbeating brain-dead organ donor. Br J Anaesth 2012; 108(Suppl. 1): i96-i107.

[3] Roig E, Almenar L, Crespo-Leiro M, et al. rest of the participants of the spanish heart transplantation registry. Heart transplantation using allografts from older donors: Multicenter study results. Heart Lung Transplant 2015; 34: 790-6.

[4] Kimura Y, Seguchi O, Iwasaki K, et al. Impact of coronary artery calcification in the donor heart on transmitted coronary artery disease in heart transplant recipients. Circ J 2018; 82(12): 3021-8.

[5] Fenton M, Mahmood A, Burch M, Simmonds J, Kuhn MA. Comparative study of pediatric coronary allograft vasculopathy between single centers in North America and United Kingdom. Transplant Proc 2018; 50(10): 1705-9.

[6] Tuzcu EM, Kapadia SR, Sachar R, et al. Intravascular ultrasound evidence of angiographically silent progression in coronary atherosclerosis predicts long-term morbidity and mortality after cardiac transplantation. J Am Coll Cardiol 2005; 45(9): 1538-42.

[7] Károlyi M, Kolossváry M, Barykowszki A, et al. Quantitative CT assessment identifies more heart transplanted patients with progressive coronary wall thickening than standard clinical read. J Cardiovasc Comput Tomogr 2019; 13(2): 128-33.

[8] Lechiancole A, Vendramin I, Sponga S, et al. Influence of donor-transmitted coronary artery disease on long-term outcomes after heart transplantation. J Am Coll Cardiol 2005; 45(9): 1538-42.

[9] Grauhan O, Sinisgalli H, Dandel M, et al. Coronary atherosclerosis of the donor heart--impact on early graft failure. Eur J Cardiothorac Surg 2007; 32(4): 634-8.

[10] Lee MS, Tadwalkar RV, Fearon WF, et al. Cardiac allograft vasculopathy: A review. Catheter Cardiovasc Interv 2018; 92(7): E527-36.

[11] Stehlík J, Kobashigawa J, Hunt SA, Reichenspurner H, Kirklin JK. Honoring 50 years of clinical heart transplantation in Circulation: In-depth state-of-the-art review. Circulation 2018; 137(1): 71-87.

© 2021 Göbölös et al.

This is an open access article distributed under the terms of the Creative Commons Attribution 4.0 International Public License (CC-BY 4.0), a copy of which is available at: https://creativecommons.org/licenses/by/4.0/legalcode. This license permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.