

# ALLOGRAFT CORONARY ARTERY THROMBOSIS: A CASE REPORT OF EARLY CARDIAC ALLOGRAFT LEFT VENTRICULAR MYOCARDIAL INFARCTION

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## Introduction

Cardiac allograft dysfunction is a major cause of morbidity and mortality in the early post-transplantation period. This is a critical condition that requires prompt diagnosis and management. We present the case of a 57-year-old man with ischemic cardiomyopathy who underwent cardiac transplantation and developed a rare case of coronary artery thrombosis in the setting of heparin-induced thrombocytopenia and thrombosis syndrome (HITTS) within the first 2 postoperative weeks. Transmural myocardial infarction (MI) was initially noted on cardiac magnetic resonance (CMR) imaging as regional left ventricular wall motion abnormalities and transmural hyperenhancement after gadolinium administration, prompting further evaluation of the coronary circulation with angiography.

## Case Report

A previously healthy 57-year-old man presented to the ER in cardiogenic shock. Cardiac enzymes and electrocardiography demonstrated an anteroseptal non-ST-segment elevation myocardial infarction (NSTEMI). Emergent cardiac catheterization revealed triple-vessel coronary artery disease, and percutaneous coronary interventions were pursued. Despite these actions, the patient's hemodynamic condition continued to deteriorate, requiring the placement of extracorporeal membrane oxygenation (ECMO) as a bridge to left ventricular assist device (LVAD).

The patient remained on LVAD support for 7 months prior to undergoing orthotopic heart transplantation. Table 1 describes donor and recipient characteristics. Prophylactic treatment was instituted for cytomegalovirus mismatch. Cytotoxic T-cell and B-cell testing was negative. The perioperative and immediate postoperative periods were uncomplicated.

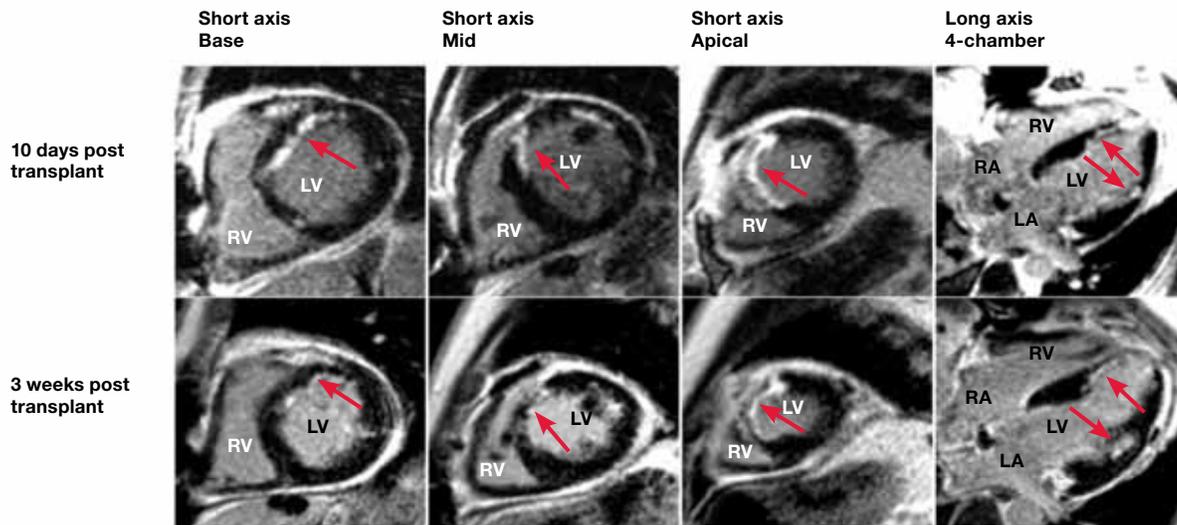
During the first postoperative week, the patient developed right upper-extremity swelling and tenderness; Doppler ultrasound revealed deep vein thrombosis in the right cephalic and innominate veins surrounding a central line, and heparin infusion was initiated. The patient remained hemodynamically stable. A routine right ventricle endomyocardial biopsy (MB) on the eighth postoperative day revealed moderate (grade 2R) rejection, and pulse steroid therapy was begun in addition to our standard immunosuppression therapy (mycophenolate mofetil, tacrolimus, and prednisone) that had been started early postoperatively. It is our practice to follow up cases of moderate rejection with functional studies for further adjustment of immunosuppressive therapy.<sup>1</sup> Two-dimensional echocardiography revealed mild LV hypokinesia without overt focal wall motion abnormalities and an ejection fraction (EF) of 45% to 49%. However, incomplete visualization of the endocardium precluded accurate wall motion evaluation, and therefore CMR imaging was obtained. Left ventricular volumetric measurements included an end diastolic volume of 164 cc/m<sup>2</sup>, an end systolic volume of 93 cc/m<sup>2</sup>, and an ejection fraction of 43%. The left ventricle was diffusely

Donor	Age	19
	Gender	Male
	PMH	None
	Blood type	A Rh+
	CMV status	Positive
	Cause of Death	Traumatic brain injury
	Echocardiogram	EF of 60% with normal findings
	Donor ischemia time	255 minutes
Recipient	Age	57
	Gender	Male
	PMH	Ischemic cardiomyopathy on LVAD support
	Blood type	A Rh-
	CMV Status	Negative

CMV: cytomegalovirus; LVEF: left ventricle ejection fraction; LVAD: left ventricular assist device; PMH: past medical history; Rh: Rhesus factor

**Table 1.** Patient and donor characteristics

hypokinetic with complete akinesia of the anteroseptum. Delayed-enhancement CMR revealed near-transmural hyperenhancement on the anteroseptal wall with subendocardial extension to the inferoseptal and anterior walls, suggesting MI in the territory of the left anterior descending (LAD) coronary artery. There was a separate area of subendocardial hyperenhancement in the anterolateral wall corresponding to left circumflex coronary territory (Figure 1). A follow-up select coronary angiogram demonstrated partially occluding intracoronary thrombi in both the LAD and left circumflex arteries (Figure 2A). Clopidogrel (75 mg daily) was added to low-dose aspirin as anticoagulation therapy.



**Figure 1.** Delayed-enhancement cardiac magnetic resonance with long axis 4-chamber view. (A) Postoperative day 10, and (B) 3 weeks post-transplantation showing near transmural infarction (arrows) of the anteroseptum with subendocardial extension to the anterior wall consistent with left anterior descending artery distribution. There is also a separate infarction in the anterolateral wall consistent with left circumflex artery distribution. These findings remain unchanged throughout the time points imaged. LA: left atrium; LV: left ventricle; RA: right atrium; RV: right ventricle

On the day of the coronary angiogram, the patient's platelet count reached 113 K/ $\mu$ L after trending downward from 200 K/ $\mu$ L measured 4 days prior. The platelet count reached a nadir of 77 K/ $\mu$ L the following day. Heparin antibodies were ordered and found to be positive (2.747 optical density units). Heparin was immediately discontinued, and intravenous bivalirudin infusion at 0.15 mg/kg per hour — and adjusted to achieve an activated partial thromboplastin time of 1.5 to 2.5 times baseline — was started for anticoagulation treatment during hospitalization and administered for a total of 2 weeks. The patient was discharged on postoperative day 29 with triple therapy immunosuppression as mentioned above, and anticoagulant/antithrombotic therapy consisting of clopidogrel (75 mg daily), aspirin (81 mg daily), and subcutaneous fondaparinux and warfarin (7.5 mg and 5 mg daily, respectively). Fondaparinux was discontinued early after discharge, and anticoagulation therapy was continued with warfarin for a 12-month period, with a goal international normalized ratio of 2:3.

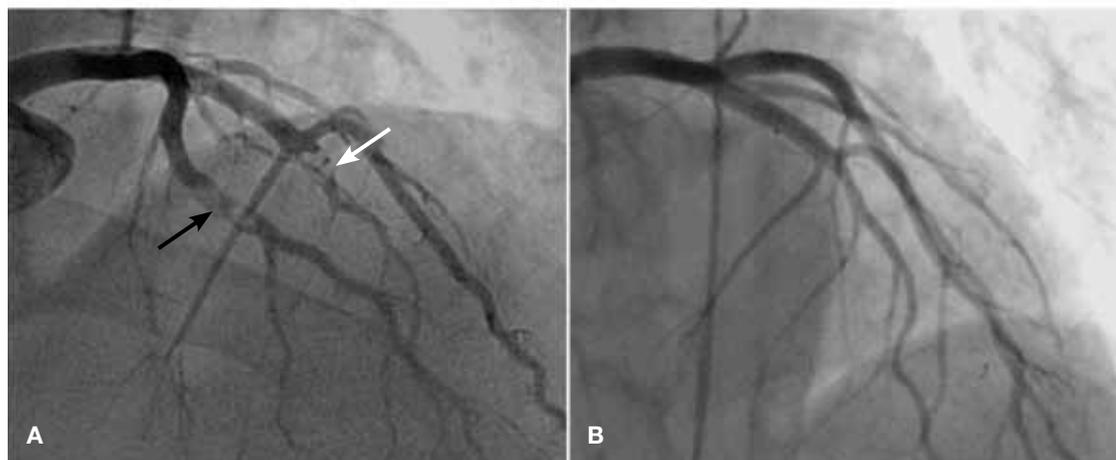
Repeat CMR imaging at 3 weeks (Figure 1) and 3 months after transplantation continued to demonstrate persistent

hyperenhancement in both the LAD and LCX distributions, representing ischemic scar. Follow-up cine coronary angiography 5 months later showed complete resolution of intracoronary thrombi (Figure 2B).

## Discussion

The primary causes of early cardiac allograft dysfunction include donor characteristics (e.g., brain death in organ donor), the effects of ischemia with organ preservation, allograft rejection, severe pulmonary hypertension, and pericardial tamponade.<sup>2</sup> Coronary allograft vasculopathy (CAV) is a common complication of heart transplantation and may be accompanied by intracoronary thrombus formation, but clinically significant effects of this disease most commonly become evident years after transplantation.<sup>3</sup> There is a relationship between CAV and the development of intracoronary thrombi, but it has only been shown several months after transplantation at the earliest<sup>4</sup>

Few cases of coronary artery thrombosis in the early post-transplantation period have been reported, and all of these have been associated with disease or aberrant anatomy of the donor



**Figure 2.** Coronary cine angiographies showing cranial right anterior oblique views at different time points. (A) Imaging on postoperative day 15 showed multiple intracoronary thrombi with preserved distal flow (black arrow  $\Rightarrow$  thrombus in the left circumflex; white arrow  $\Rightarrow$  mid-left anterior descending). (B) Follow-up angiography 6 months after transplantation showing complete resolution of thrombi.

coronary arteries.<sup>2,5,6</sup> Although in our case, the donor's coronary arteries were not evaluated due to young age, echocardiography performed on the donor showed no wall motion abnormalities and an ejection fraction of 60%. It would be unlikely that the coronary thrombosis suffered by our patient was a result of pre-existing coronary pathology and is more likely related to the development of heparin-induced thrombocytopenia (HIT) in association with a prolonged ischemic time of the cardiac allograft.

HIT is a complication of unfractionated heparin administration, with thrombocytopenia developing typically within 1 week of initiating therapy. It results from an immune-triggered appearance of antibodies that recognize complexes of heparin and platelet factor 4 on the surface of platelets, as well as complexes of heparin-like molecules and platelet factor 4-like proteins on endothelial cells. This disorder was formerly designated as HIT type 2 to distinguish it from nonimmune-mediated heparin-induced thrombocytopenia, known as HIT type 1.<sup>7</sup> The platelet count may drop by 50% or fall below 150,000, but ultimately it produces a prothrombotic state, and around 1% of these patients will manifest with heparin-induced thrombocytopenia and thrombosis (HITT) syndrome with unpredictable venous and arterial thrombosis.<sup>8</sup>

HITT syndrome is a fairly common cause of intravascular thrombosis in cardiac transplant recipients, occurring in up to 10% of such patients.<sup>9</sup> However, involvement of the coronary circulation is extremely rare; in the setting of postcardiac transplantation HITT syndrome, coronary artery thrombosis has only been reported in association with percutaneous coronary interventions and to our knowledge has not been reported as a spontaneous occurrence.<sup>10,11</sup>

## Conclusion

Our patient suffered intracoronary thrombosis early after cardiac transplantation in the absence of overt pre-existing coronary artery disease. The nature of this event was most likely multifactorial and due to prolonged ischemia time, donor brain death, cytomegalovirus mismatch, and acute allograft cellular rejection. All of these are known to cause endothelial dysfunction,<sup>3,12-14</sup> which in the presence of HITT syndrome might have collectively precipitated the formation of intracoronary thrombi. Irrespective of the etiology, CMR imaging with late gadolinium enhancement detected an evolving transmural MI and guided the management of our patient. CMR imaging has proved to be effective in the recognition of MI<sup>15,16</sup> and is being actively investigated as a noninvasive tool to evaluate and delineate potential causes of LV cardiac allograft dysfunction.<sup>1,17-19</sup> It will continue to play an increasingly important role in follow-up evaluation of the heart transplant patient.

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