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CASE REPORT
Coronary heart disease

Case report of a coronary artery-right ventricular fistula following repeat endomyocardial biopsies in a heart transplant patient

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Background Endomyocardial biopsy (EMB) remains the gold standard for cellular rejection surveillance in heart transplant recipients. Coronary artery fistula formation is a rare late and potentially catastrophic complication of repeated endomyocardial biopsies, without contemporary evidence on incidence or management.

Case summary A 47-year-old male was found to have a fistula between his right ventricle and his left anterior descending artery on an angiogram that was performed as a part of regular screening of coronary allograft vasculopathy. Given the low shunt fraction, asymptomatic nature, and lack of guidelines on definitive management, the patient is undergoing conservative management with regular surveillance.

Discussion Coronary artery fistulas were once thought to be rare complications of repeated EMB, but the true prevalence is likely to be higher than previously believed. Ideal treatment and monitoring is unknown given the relative rarity of the condition.

Keywords Endomyocardial biopsy • Coronary artery fistula • Case report

Learning points:

- Coronary artery fistula caused by repeat endomyocardial biopsy is more common than previously believed.
- Ideal treatment strategy is still unknown in these patients.
- Closure is reasonable if symptomatic or with haemodynamically significant shunts.

Introduction

Endomyocardial biopsy (EMB) is the gold standard method for monitoring for allograft cellular rejection in heart transplant patients.[1] Overall, it is an immediately safe and well-tolerated procedure with a low complication rate.[2] Endomyocardial biopsy is performed using a bioptome inserted through either the right internal jugular or right femoral vein, and biopsy specimens are taken from the

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interventricular septum using either fluoroscopic or echocardiographic guidance to ensure a safe location for biopsy.[3] Immediate risks include access site complications, transient arrhythmias, valvular injury (particularly the tricuspid valve), and pulmonary embolism. A complication of biopsies from the interventricular septum is the formation of a coronary artery fistula (CAF).[3]

The ideal management of patients who develop CAF is unclear because of the lack of major society guidelines addressing the condition, as well as the relative rarity of the condition.

Timeline

Transplant (Day 0)	Orthotopic heart transplant with bicaval anastomosis; surgery uncomplicated
4 days	Post-op course complicated by hypotension, required emergent sternal exploration; bovine patch repair of Superior Vena Cava-Right Atrial anastomosis
2 weeks	Right Heart Catheterization (RHC)/ Endomyocardial biopsy (EMB); eight samples; all negative for acute rejection (Grade 0/0R); C4D immunofluorescent stain negative
3 weeks	RHC/EMB; seven samples; all negative for acute rejection (Grade 0/0R)
4 weeks	RHC/EMB; four samples; all negative for acute rejection (Grade 0/0R)
6 weeks	RHC/EMB; four samples; all negative for acute rejection (Grade 0/0R)
7 weeks	RHC/EMB; four samples; three sample negative for acute rejection (Grade 0/0R)
9 weeks	RHC/EMB; four samples; all negative for acute rejection (Grade 0/0R)
11 weeks	RHC/EMB; five samples; all negative for acute rejection (Grade 0/0R)
13 weeks	RHC/EMB; four samples; all negative for acute rejection (Grade 0/0R)
9 months (6 m after last EMB)	RHC/EMB; four samples; with focal mild acute cellular rejection (Grade 1A/1R)
14 months 2 weeks (5 months 2 weeks after last EMB)	Coronary angiogram, RHC, no EMB performed because of fistula finding

Case presentation

A 47-year-old male patient presented for his first coronary allograft vasculopathy surveillance angiogram after undergoing an orthotopic heart transplant with bicaval anastomosis 14 months prior. He had undergone routine EMB as part of his cellular rejection surveillance, with his last biopsy being 5.5 months prior to the current evaluation. At his current presentation, he had no complaints and was without functional limitations, and the physical exam was unrevealing.

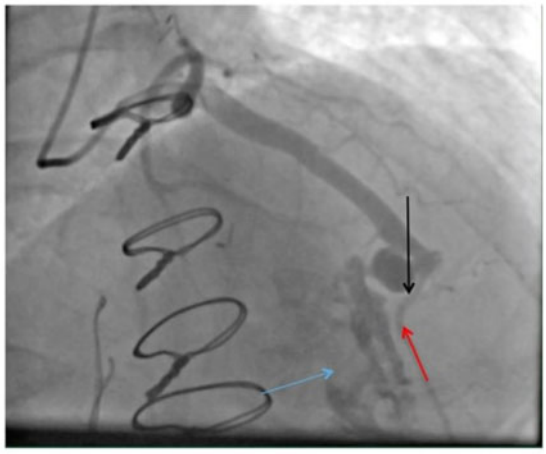


Figure 1 Coronary angiogram showing fistulous connection (black arrow), with aneurysmal segment of left anterior descending artery (red arrow), and opacification within the right ventricle (blue arrow).

The patient was diagnosed with hypertrophic cardiomyopathy in childhood and had failed medical therapy and progressed to end-stage heart failure complicated by severe pulmonary hypertension requiring transplantation. In the immediate perioperative period, he underwent repair of the superior vena cava-right atrial anastomosis following the development of super vena cava syndrome due to central venous catheter-associated superior vena cava thrombus. Following hospital discharge after his transplant, he had been doing well. His immunosuppressive regimen was a combination of mycophenolate mofetil and tacrolimus since transplant, with regular monitoring of his levels. He did not have any angina, heart failure symptoms, or arrhythmias. He took all of his medications including his immunosuppressive regimen without major adverse effects.

As part of routine institutional post-transplant rejection surveillance, he had undergone regular EMB with a 9-Fr Scholten Novatome (Scholten Surgical Instruments, Inc., Lodi, CA, USA) without any complications (see Timeline). There was no obstruction at the level of the previous superior vena cava-right atrial anastomosis repair, and therefore biopsies were done predominately from a right internal jugular vein approach, with two performed via right femoral vein access based on operator preference. Pathology did not reveal any acute cellular rejection in any of the biopsy samples in the immediate post-operative period. His last biopsy was 9 months post-transplant and did show mild focal acute rejection (Grade 1A/1R); however, his immunosuppressive regimen was not changed, and there was preserved allograft function at this time. There had been no immediate complications following any of the previous biopsies, and post-operative echocardiography was routine. During each biopsy, up to eight specimens were obtained from the interventricular septum using fluoroscopic guidance and provocation of premature ventricular contractions to ensure a septal location for each biopsy. Pathology from all specimens revealed myocardial tissue and no samples contained adipose tissue or fibroadipose tissue consistent with

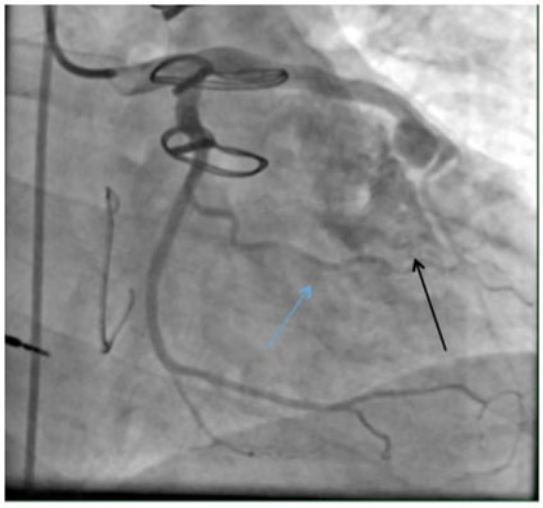


Figure 2 Coronary angiogram showing fistulous connection between left anterior descending artery and right ventricle with left anterior descending artery aneurysm and right ventricle opacification (blue arrow).

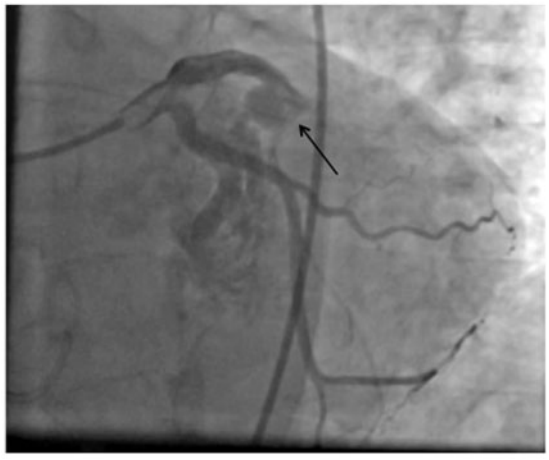


Figure 3 Coronary angiogram showing the left anterior descending artery-right ventricle fistula (black arrow).

an epicardial site of biopsy, nor were there were any reports of vasculature within the pathology specimen. There had been some biopsy specimen that showed signs of the previous biopsy.

Prior to transplant, there was no known coronary artery disease of the allograft, and at transplant, the specimen showed no disease nor coronary calcifications.

The patient underwent a scheduled coronary angiogram, which revealed an aneurysmal, dilated left anterior descending artery (LAD) with evidence of fistula formation to the right ventricle (RV) in the mid-segment (*Figures 1–3*). The left circumflex and right coronary arteries were free of coronary artery disease.

Following the angiogram, a right heart catheterization was performed, which showed a superior vena cava oxygen saturation of 70%, a right atrial oxygen saturation of 70%, and a right ventricular oxygen saturation of 84.5%. The aortic oxygen saturation was 97.8%. A step-up in oxygen saturation from the right atrium to the right ventricle confirmed the diagnosis of a left-to-right fistula into the right ventricle, and Qp:Qs was 1.4. Computed tomography coronary angiogram confirmed the diagnosis of an aneurysmal LAD with an LAD-RV fistula.

Given his lack of chest trauma, normal coronary arteries in allograft prior to transplantation, and multiple previous biopsies taken from the interventricular septum, it is exceedingly likely that the fistula is a late sequela of repeated endomyocardial biopsies.

Management

He did not have any signs of right ventricular overload on the transthoracic echocardiogram, indicating that he was well compensated in spite of the left-to-right shunting. With a Qp:Qs <1.5, his shunt was not considered to be haemodynamically significant at that time. Because he was asymptomatic, had preserved cardiac function, and had a complicated surgical history with multiple intrathoracic and cardiac surgeries, conservative management was advised. After discussion with the patient, it was mutually decided to continue our institutional post-rejection surveillance protocol of monitoring for acute rejection with EMB and annual left heart catheterization for coronary allograft vasculopathy screening for the first 5 years post-transplant. During cardiac catheterization, we will perform a surveillance shunt evaluation with calculation of Qp:Qs. If the patient develops any signs or symptoms of haemodynamically significant shunt, we would offer endovascular closure with percutaneous coiling vascular plug, or covered stents. These percutaneous strategies have been previously successfully utilized and published strategies for closure.[4–6] He has remained symptom-free throughout his follow-up to this point.

Discussion

Previously believed to be a rare complication of EMB with a rate of 5–8%,[7,8] newer data reveal that CAF are more common than this. A case series of 432 patients who had undergone orthotopic heart transplant showed that the rate of coronary artery-right ventricular fistula, most likely to be a complication of EMB, to be 12.5%. The majority of patients were asymptomatic and had benign clinical courses.[9]

The potential causes of coronary artery fistula formation following EMB are hypothesized to be related to enhanced angiogenesis from cardiac transplantation, surgical trauma, or secondary to EMB.[9] The location of the fistula in this case, from the mid-LAD to the RV, makes it likely to be related to previous EMB, as the RV septum is the preferred site of biopsy. The course of the LAD along the interventricular septum is in close proximity to the RV septal biopsy sites. There may have been incidental septal branch involvement in a previous biopsy (or biopsies) that ultimately contributed to the fistula seen in this case. The frequency of EMB in this patient, while necessary, again increases the likelihood that the biopsies played a causative role.[3,7]

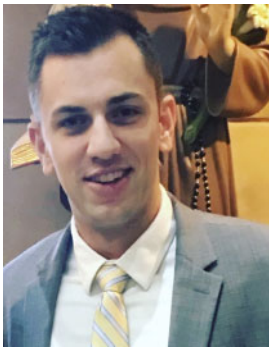
Another possible cause of CAF is accidental advancement of the bioptome into the coronary sinus, which angiographically can appear to be in a similar position as the right ventricular outflow tract; however, this is unlikely in this case, as it would be rare for this to cause a LAD-RV fistula.[10]

Despite the lack of pathology showing adipose tissue or blood vessels, there is a possibility that there were fragments of blood vessels within the biopsy specimen that were not visualized pathologically. We hypothesize that there was incidental involvement of a small septal branch of the LAD involved in a previous biopsy (or biopsies) that ultimately contributed to the large fistula that was seen in this patient.

While there are no guidelines regarding management, previous criteria used for closure have been Qp:Qs >1.5, or any symptoms that develop attributable to the fistula: coronary steal, right ventricular overload, embolic phenomenon, or mass effect on side branches.[5,11] Data on the management of this condition are derived mainly from patients with congenital coronary artery fistulae. In these cases, closure is recommended on a case-by-case basis, with careful review by a heart team.[12] Options for management include conservative management, surgical closure, or percutaneous intervention. There has been at least one case report of a successful closure of an LAD-RV fistula in a paediatric heart transplant patient using a vascular plug.[4] Percutaneous coiling has successfully been performed to close coronary artery fistulae that have significant left-to-right shunts.[6]

Coronary artery fistula is a complication of repeated EMB in transplanted hearts. Once believed to be a rare complication, CAF is being identified more commonly and are likely to be more prevalent than previously thought. Despite the use of fluoroscopic and/or echocardiographic guidance, fistulas remain a feared complication of EMB. Because there are no major guidelines on the management of CAF, these patients benefit from a shared-decision making strategy including risk–benefit discussion of closure options or conservative management if the fistula is small, asymptomatic, and the patient is at a low risk of complications.

Lead author biography



Vince Siebert is a first year cardiology fellow at Loyola University Medical Center. Born and raised in Illinois, he completed his medical school at the University of Illinois College of Medicine-Peoria before completing Internal Medicine residency at Baylor College of Medicine. He plans on pursuing a career in interventional and structural cardiology and is interested in teaching medical students and residents.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

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We would like to graciously thank the patient for giving his consent to share his case.

Slide sets: A fully edited slide set detailing these cases and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

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