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INTERMEDIATE

CASE REPORT: CLINICAL CASE SERIES

Symptomatic Presentation of Acute Myocardial Infarction in Heart Transplantation Patients

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ABSTRACT

Patients with acute myocardial infarction with a history of an orthotopic heart transplantation rarely present with classic anginal symptoms, secondary to cardiac denervation. We present 2 cases, the first of a patient with a ST-segment elevation myocardial infarction and the second who presented with a non-ST-segment elevation myocardial infarction. Both patients presented with typical symptoms and were treated with percutaneous coronary intervention. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2021;3:400–6) © 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/).

CASE 1

A 32-year-old man with a history of hyperlipidemia (HLD) and ongoing smoking had an orthotopic heart transplantation (OHT) performed 10 years earlier for nonischemic cardiomyopathy. The patient's donor was a 25-year-old man with a 3.5-h ischemic time who died secondary to a head trauma. The patient had an episode of cytomegalovirus infection early post-transplantation and 1 episode of post-transplantation rejection (grade 2, cell-mediated) that were both treated successfully. He has been on tacrolimus 4/5 mg twice daily and mycophenolate mofetil 1 g twice daily. Surveillance coronary angiography (CAG) 2 years earlier revealed cardiac allograft vasculopathy (CAV) with a focal 40% to 50% lesion of the proximal to mid-left circumflex coronary artery (**Figure 1**). He presented currently with new-onset, crushing chest pain accompanied by diaphoresis and shortness of breath. A 12-lead electrocardiogram revealed an acute inferior ST-segment elevation myocardial infarction (STEMI) (**Figure 2**). Emergent cardiac catheterization revealed a thrombotic occlusion of the left circumflex artery (**Figure 3**, Video 1). Successful aspiration thrombectomy and

LEARNING OBJECTIVES

- To understand the pathophysiology of a transplanted heart. Because of complete cardiac denervation in these patients, MI and CAV present with no symptoms or can have atypical presentation(s).
- To understand that in patients with a history of OHT, early revascularization in patients presenting with an MI can have a mortality advantage.
- To have the knowledge of appropriate and applicable PCI techniques, including use of drug-eluting stents in these patients.

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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.

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coronary stenting using a drug-eluting stent was performed (**Figure 4**, Video 2). His symptoms and electrocardiographic changes resolved post-procedure (**Figure 5**). High-sensitivity troponin peaked at 1,230 ng/ml. At 1-month follow-up, the patient remained stable and had successfully quit smoking.

CASE 2

A 52-year-old woman with a history of poorly controlled diabetes mellitus, HLD, and smoking had an OHT in 2009 for a history of ischemic cardiomyopathy. The patient's donor was a 46-year-old male patient who died secondary to a cerebrovascular accident; the ischemic time was 4.1 h. Post-transplantation, the patient had 1 episode of cytomegalovirus infection that was successfully treated with no episodes of cellular or humoral rejection. She has been on tacrolimus 5 mg twice daily and mycophenolate mofetil 500 mg twice daily. Surveillance CAG in 2016 revealed CAV with mild disease in the mid-left circumflex artery, a 70% focal lesion in the obtuse marginal 1 branch (**Figure 6**) vessel and mild disease in the right coronary artery with a normal stress echocardiogram in 2019. She presented currently with symptoms of sudden onset chest pain that awoke her from sleep. An electrocardiogram revealed sinus tachycardia with no acute ischemic changes (**Figure 7**). A bedside echocardiogram revealed apical, peri-apical, and septal hypokinesis with inferior wall akinesis. Initial high-sensitivity troponin was 216 ng/dl. She underwent an urgent CAG. This demonstrated a proximal 90% stenosis of the left anterior descending artery, a 50% to 60% stenosis of the mid-portion of the left circumflex artery, unchanged lesion in the obtuse marginal 1 branch (**Figure 8**, Video 3), and a subtotal occlusion of the small right coronary artery (**Figure 9**). Based on the transthoracic echocardiographic findings and the angiographic appearance, the lesion in the left anterior descending artery was the culprit for this clinical presentation. This was further confirmed during angioplasty because the patient experienced exacerbation of her chest pain during balloon inflation(s) to the proximal left anterior descending artery and experienced resolution of symptoms once the stent was placed. (**Figure 10**, Video 4).

DISCUSSION

CAV is characterized as an accelerated, diffuse fibro-proliferative process that affects the entire epicardial and intramural coronary tree, which leads to eventual allograft ischemia. At 10 years post-transplantation, the prevalence is estimated at approximately 50% and is the leading cause of morbidity and mortality (1). Development of CAV is believed to be an inflammatory response to both immune (immunosuppressive drugs, viral infections, human leucocyte antigen-directed antibodies) and nonimmune risk factors, including smoking, HLD, diabetes mellitus, and donor age (2). Superimposed atherosclerotic lesions can develop later in the disease process in these patients (3), and they have the potential to manifest as MI.

Cardiac transplantation results in transection of the post-ganglionic neuronal axons innervating the heart, which results in axonal degeneration and total cardiac denervation (1). In 1991, Stark et al. (4) first reported evidence of re-innervation in patients who presented with classic symptoms of angina, along with evidence of MI in patients who underwent OHT. Re-innervation, which is usually incomplete and heterogenous, was reported to start in the second year and could continue up to 15 years post-surgery (1). Some patients (10% to 30%) were reported to have re-innervation; these patients usually presented with typical symptoms (5).

ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndrome

CAG = coronary angiography

CAV = cardiac allograft vasculopathy

HLD = hyperlipidemia

MI = myocardial infarction

NSTEMI = non-ST-segment elevation myocardial infarction

OHT = orthotopic heart transplantation

PCI = percutaneous coronary intervention

STEMI = ST-segment elevation myocardial infarction

FIGURE 1 Previous Angiography With Moderate Stenosis of Mid-Left Circumflex Coronary Artery

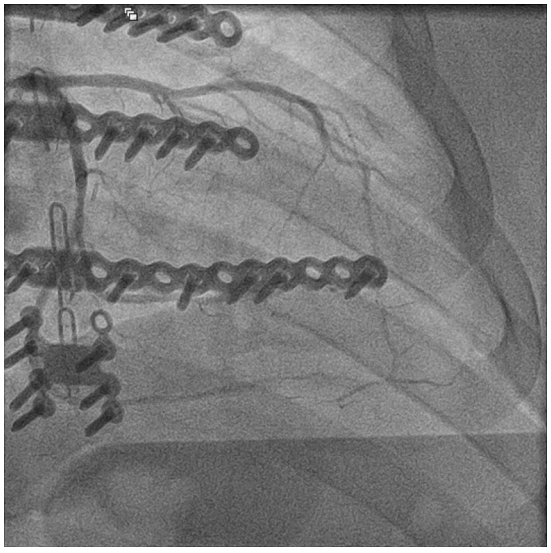
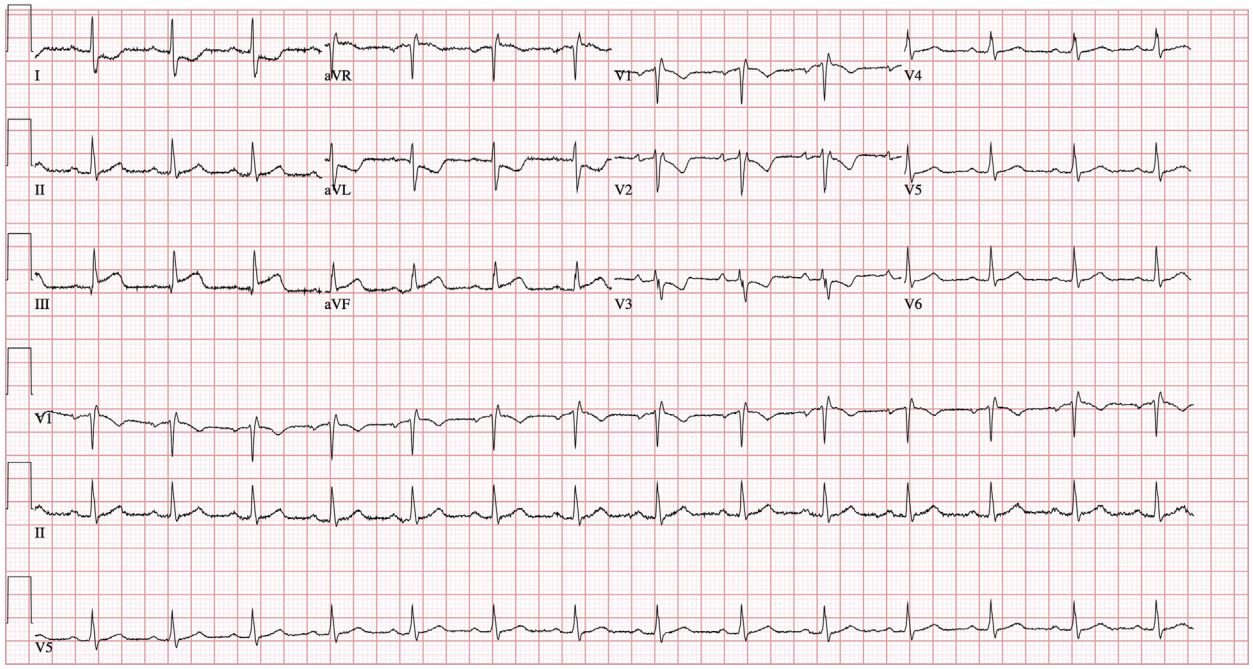
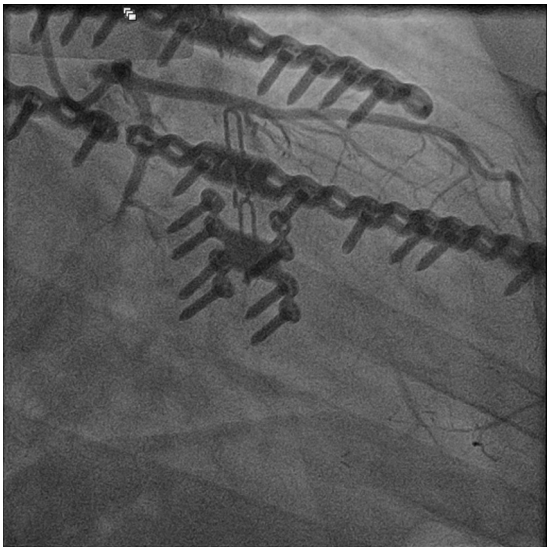


FIGURE 2 Electrocardiogram Demonstrating Inferior ST-Segment Elevation Myocardial Infarction



Thus, most patients who have undergone OHT and who experience acute coronary syndrome (ACS) usually are asymptomatic or have atypical presentations with dyspnea, fatigue, syncope, and heart rate or rhythm changes (6). In a study of 329 patients post-OHT, only 2 of 22 patients who sustained an MI actually presented with classic symptoms of chest pain (7). Therefore, the true incidence of ACS in patients with OHT is not known, and MI is usually diagnosed in the subacute or chronic phase, with patients presenting with graft failure, heart failure syndrome, or sudden cardiac death.

FIGURE 3 Angiography With Complete Occlusion of Left Circumflex Coronary Artery



In the absence of reliable symptoms in most patients who have undergone OHT, the detection of CAV in early stages is important. Routine surveillance in patients with heart transplantation has thus been recommended. CAG, along with use of intracoronary imaging, is considered the gold standard for diagnosis (6) of CAV. Noninvasive imaging modalities like exercise stress tests, cardiac computed tomography angiography, and cardiac magnetic resonance are also routinely used.

Definitive therapy for patients presenting with advanced CAV would be to offer a repeat OHT; however, because of the paucity of available hearts and the increased associated morbidity and mortality with re-do surgery, this is usually reserved for selective candidates (8). Revascularization options include

percutaneous coronary intervention (PCI) or coronary artery bypass grafting.

PCI in advanced CAV is feasible with high procedural success. Earlier angiographic success with balloon angioplasty and use of bare metal stents was noted but has been associated with high rates of restenosis (6,8). In comparison, drug-eluting stents, in particular, second-generation stents, have lower rates of in-stent restenosis and target vessel revascularization (3). However, because of the diffuse and progressive nature of the disease, stent placement has shown to not affect graft survival or confer a mortality benefit and is mostly considered palliative (6,8).

In contrast, PCI may be more effective in a subset of patients who present with symptoms of ischemia due to focal lesions of the proximal vessels (9). Shah et al. (10) analyzed a total of 1,621 patients who were discharged with a history of OHT and an ACS diagnosis (10). These patients (66%) had a diagnosis of NSTEMI and unstable angina, and the remaining 34% were discharged with a diagnosis of STEMI. Patients

FIGURE 4 Left Circumflex Artery, Status Post-Angioplasty

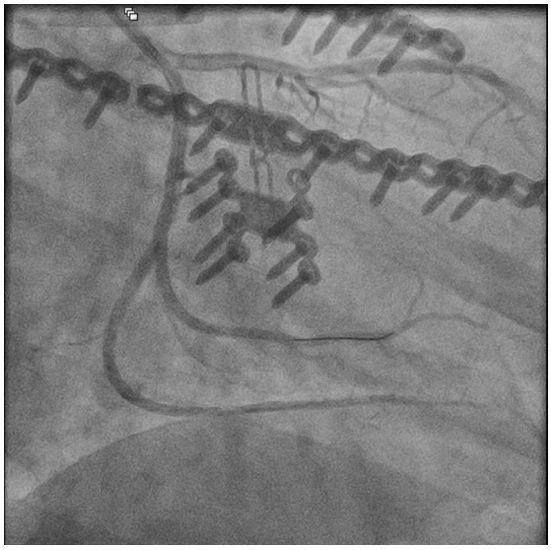


FIGURE 5 Post-Stenting Electrocardiogram With Resolution of ST-Segment Elevation

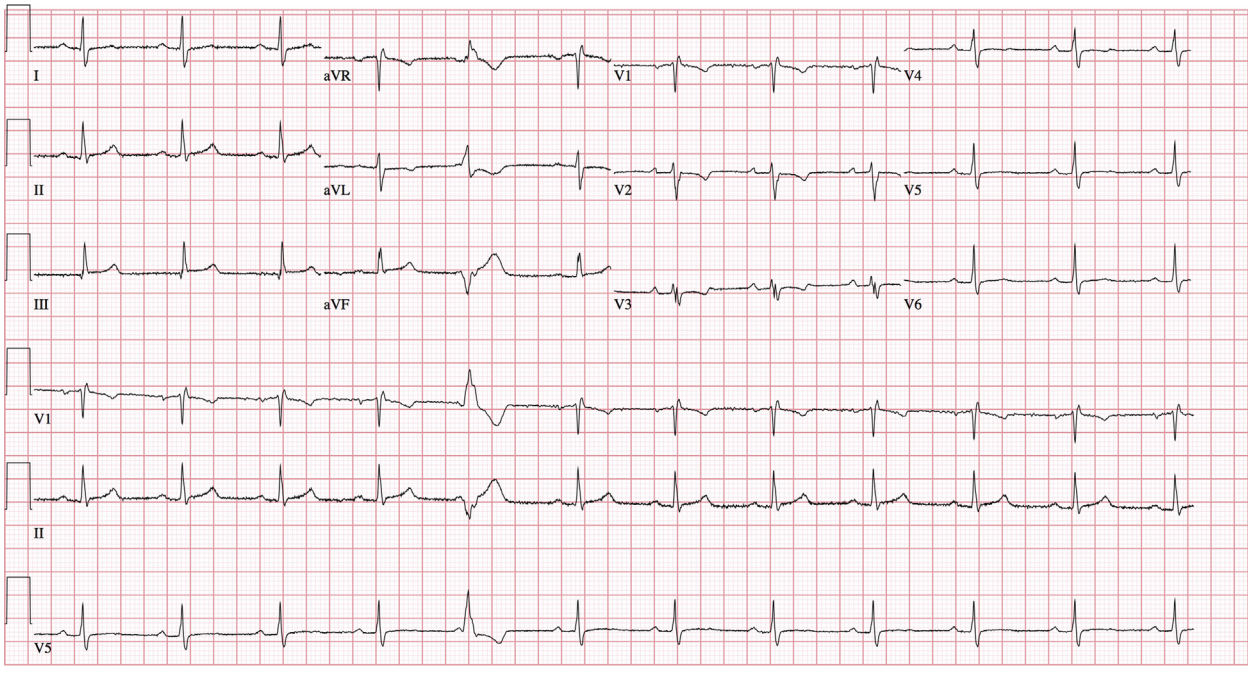
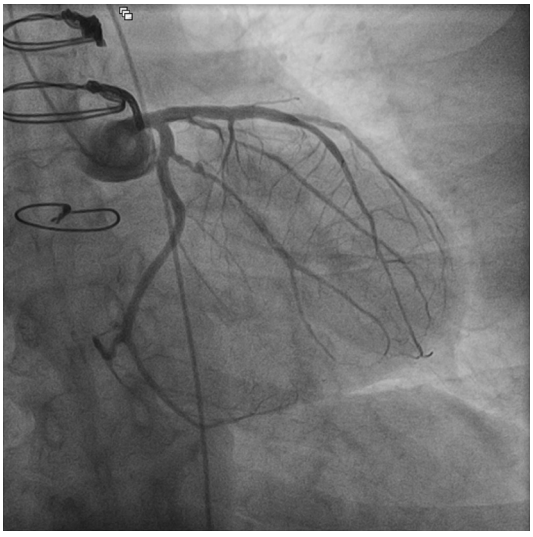


FIGURE 6 Prior Angiography Showing Previous Left Circumflex Artery/Obtuse Marginal 1 Disease



with a diagnosis of MI and those who underwent revascularization had a significantly lower in-hospital mortality (7%) compared with those who did not (19%). Overall, there appears to be a mortality advantage to early revascularization in patients who present with ACS.

CONCLUSIONS

In conclusion, CAV remains the most frequent long-term complication of OHT and can frequently present as ACS. Early recognition is often difficult due to the de-innervated heart. In absence of ischemic symptoms, recognition of an ACS can be challenging and often the cause of a missed or delayed diagnosis of MI. New findings on transthoracic echocardiograms, including a decline in function or presentation with new, atypical symptoms, should trigger workup for CAV and prompt appropriate medical or interventional treatment.

FIGURE 7 Baseline Electrocardiogram With Nonspecific ST-Segment Abnormalities

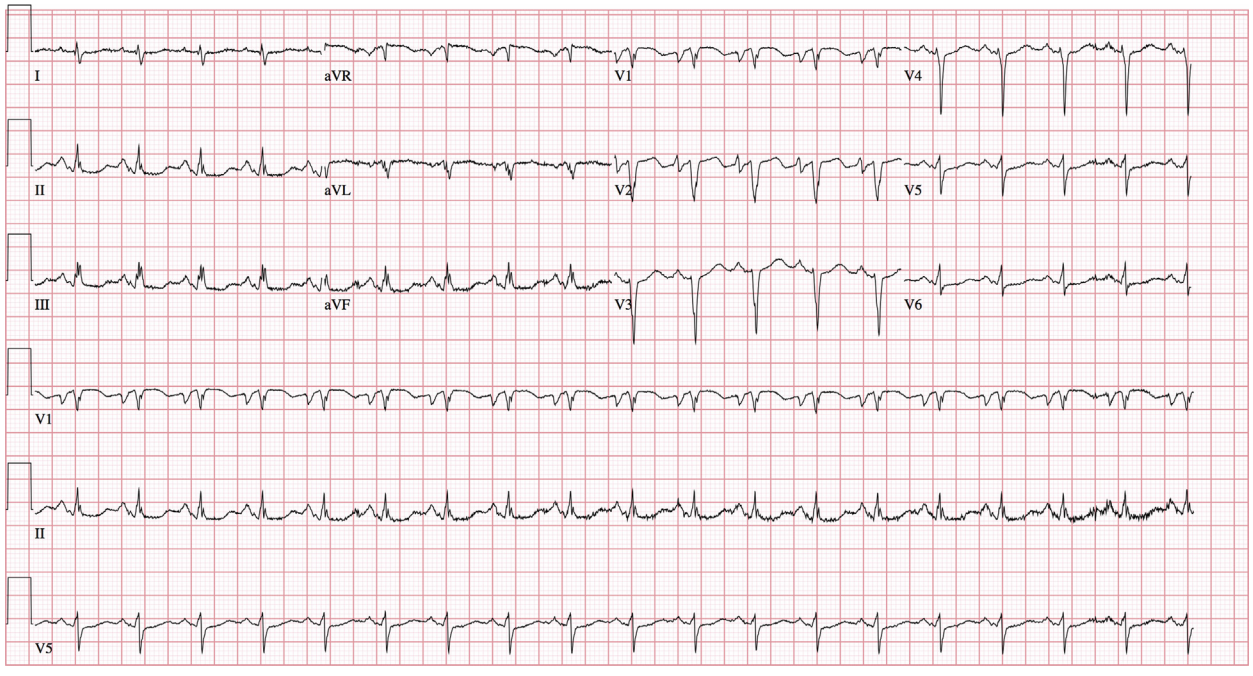


FIGURE 8 Pre-Stenting Left Coronary Angiography

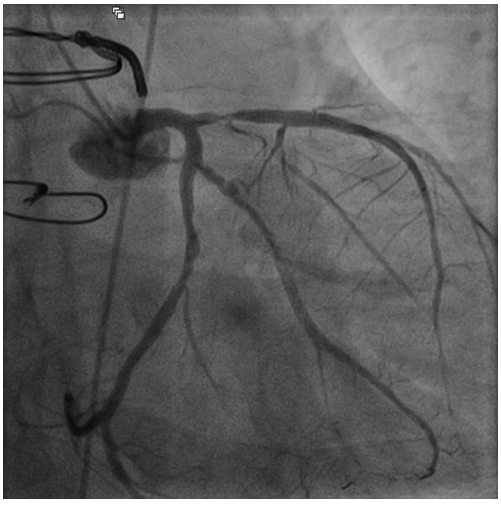


FIGURE 9 Pre-Stenting Right Coronary Angiography

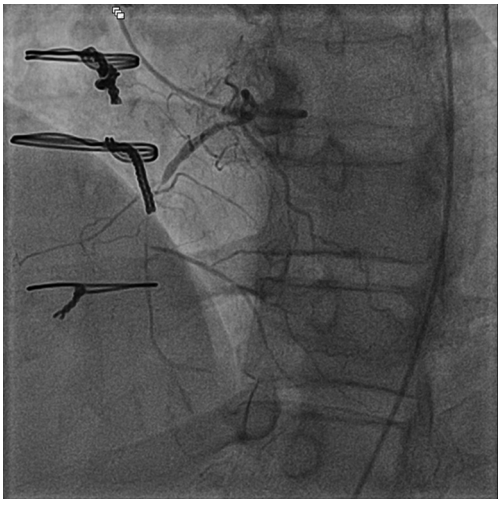
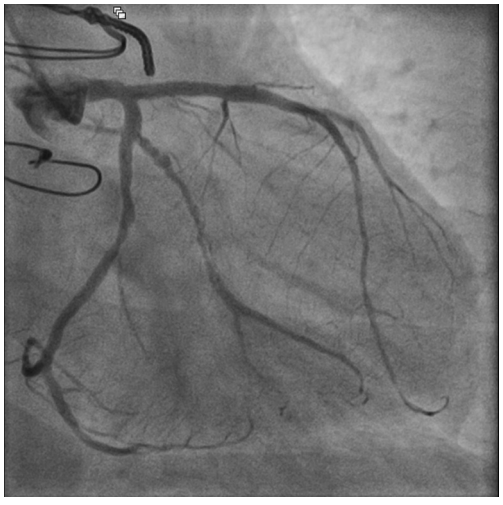


FIGURE 10 Post-Left Anterior Descending Stenting Angiography



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REFERENCES

1. Grupper A, Gewirtz H, Kushwaha S. Reinnervation post-heart transplantation. Eur Heart J 2018;39:1799–806.

2. Zimmer RJ, Lee MS. Transplant coronary artery disease. J Am Coll Cardiol Intv 2010;3:367–77.

3. Cheng R, Kobashigawa J. Transplant CAD: The role of PCI in the transplanted heart. 2016. ACC.ORG. March 2016. Available at: https://www.acc.org/latest-in-cardiology/articles/2016/03/18/08/28/transplant-cad-the-role-of-pci-in-the-transplanted-heart. Accessed July 17, 2020.

4. Stark R, McGinn A, Wilson R. Chest pain in cardiac-transplant recipients. N Engl J Med 1991;324:1791–4.

5. Aranda JM, Hill J. Cardiac transplant vasculopathy. Chest 2000;118:1792–800.

6. Lee M, Tadwalkar R, Fearon W, et al. Cardiac allograft vasculopathy: a review. Catheter Cardiovasc Interv 2018;92:E527–36.

7. Gao S, Schroeder J, Hunt S, et al. Acute myocardial infarction in cardiac transplant recipients. Am J Cardiol 1989;64:1093–7.

8. Lee M, Lluri G, Finch W, et al. Role of percutaneous coronary intervention in the treatment of cardiac allograft vasculopathy. Am J Cardiol 2018;121:1051–5.

9. Dasari T, Jorge Saucedo F, Krim S, et al. Clinical characteristics and in hospital outcomes of heart transplant recipients with allograft vasculopathy undergoing percutaneous coronary intervention: insights from National Cardiovascular Data Registry. Am Heart J 2015;170:1086–91.

10. Shah Z, Rali A, Vuddanda V, et al. Acute coronary syndromes in heart transplant recipients (from a national database analysis). Am J Cardiol 2018;122:1824–9.

KEY WORDS cardiac allograft vasculopathy, orthotopic heart transplant

APPENDIX For supplemental videos, please see the online version of this paper.