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CASE REPORT

CLINICAL CASE

Coronary Vasospasm Causing Chest Pain in Early Postoperative Heart Transplantation

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ABSTRACT

Coronary vasospasm is a rare complication after heart transplant. Due to denervation of the donor heart, patients are typically asymptomatic but may present with cardiac arrhythmias or cardiac arrest. We present a patient with a recent heart transplant who experienced chest pain and was found to have coronary vasospasm. (J Am Coll Cardiol Case Rep 2023;28:102100) 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/).

HISTORY OF PRESENTATION

A 62-year-old man who underwent heart transplant 5 months prior presented to the hospital after the sudden onset of progressive, left-sided chest pain with numbness/tingling of his left arm. The symptoms were associated with shortness of breath, diaphoresis, and lightheadedness progressing to loss of consciousness for approximately 30 seconds. He was brought in by ambulance, and upon arrival to the emergency department, he was tachycardic with heart rate 100 beats/min and blood pressure 118/81 mm Hg without significant differences between his arms. His physical examination was unremarkable with regular heart rhythm without murmurs, no tenderness upon palpation of chest wall, lungs clear to auscultation bilaterally, and extremities warm and well-perfused without edema.

LEARNING OBJECTIVES

- To recognize how coronary vasospasm may present in a patient with a recent heart transplant.
- To understand the role of immunosuppression in coronary vasospasm.

PAST MEDICAL HISTORY

The patient had a heart transplant 5 months before presentation for nonischemic cardiomyopathy. His other medical problems included type 2 diabetes mellitus and hyperlipidemia. His medications included tacrolimus, mycophenolate mofetil, prednisone, trimethoprim/sulfamethoxazole, valganciclovir, pravastatin, and nateglinide.

His immediate postoperative course after his heart transplant was uncomplicated. There was no cellular or antibody-mediated rejection noted on protocol-driven biopsies performed at 1 to 4, 6, 8, and 12 weeks after transplant. At months 4 and 5, he had noninvasive rejection surveillance with donor-derived cell-free DNA and peripheral blood gene expression profiling, which indicated no concern for rejection. Echocardiograms showed normal left ventricular

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ABBREVIATIONS AND ACRONYMS

CAV = coronary allograft vasculopathy

LAD = left anterior descending artery

function, most recently an ejection fraction of 69%. Routine coronary angiogram at week 6 post-transplant showed no epicardial allograft coronary artery disease, but on intravascular ultrasound there was a maximal intimal thickness of 0.3 mm in the mid-left anterior descending artery (LAD).

DIFFERENTIAL DIAGNOSIS

Due to the dramatic presentation with loss of consciousness in a patient early post-heart transplant, acute allograft rejection was high on the differential. Arrhythmias such as sinus pause were also considered given his syncopal symptoms. Other cardiac causes of chest discomfort and syncope, such as acute coronary syndrome or pericarditis, were entertained, but felt less likely because of denervation of the donor heart. Other noncardiac causes that were considered included aortic dissection, pulmonary embolism, pneumothorax, or peptic ulcer disease.

INVESTIGATIONS

His initial laboratory values were remarkable for troponin 0.03 ng/mL, which increased to 0.20 ng/mL on repeat. Serial electrocardiogram did not show ST-segment changes. His electrolytes, complete blood count, creatinine, and liver enzymes were normal. Chest x-ray did not show any evidence of consolidation, pulmonary congestion, or pneumothorax. D-dimer was negative. A transthoracic echocardiogram showed normal left and right ventricular function, a left ventricle ejection fraction of 65%, and no evidence of dissection in the ascending aorta. A right heart catheterization showed normal filling pressures and cardiac output, and repeat endomyocardial biopsy showed no evidence of cellular or antibody-mediated rejection. Cardiac magnetic resonance imaging did not show evidence of myocardia edema. He underwent a vasodilator myocardial perfusion stress test, which showed a 3% reversible defect in the inferior wall, consistent with a low likelihood of jeopardized myocardium.

MANAGEMENT

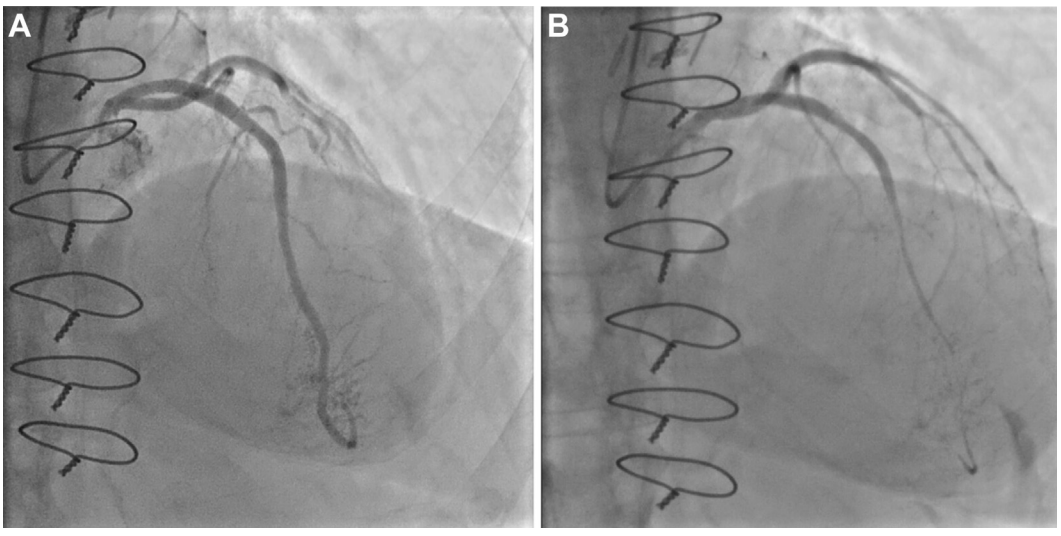
Because there was a concern for acute rejection, he received empiric pulse-dose intravenous methylprednisolone 500 mg for 3 days. However, given hemodynamic stability and once the endomyocardial biopsy demonstrated no rejection, the corticosteroids were reduced to his maintenance dose. Because of recurrent chest pain, he was started empirically on cyproheptadine 4 mg 3 times daily for presumed coronary vasospasm and was discharged home. Provocative testing for coronary vasospasm was not performed at this point in an attempt to avoid invasive procedures in the context of a low clinical suspicion for this rare diagnosis. Although calcium-channel blockers are typically first-line for coronary vasospasm, he had previously discontinued amlodipine because of lower extremity edema, and thus cyproheptadine was prescribed.

After 3 months, at 8 months post-transplant, he presented again to the hospital with chest pain and troponin peak of 0.23 ng/dL after deciding on his own to discontinue cyproheptadine because of drowsiness. He underwent a coronary angiogram with reactivity testing, which revealed minor irregularities in the mid-to-distal LAD, severe coronary vasospasm with complete obliteration of his mid-to-distal LAD with administration of intracoronary acetylcholine (**Figure 1**), and reproduction of his characteristic chest pain. Coronary vasospasm was resolved with administration of intracoronary nitroglycerin. Because calcium-channel blockers are considered first-line therapy for coronary vasospasm,[1] amlodipine 5 mg daily was started; he was willing to reattempt this agent given that the prior intolerance of lower extremity edema was not severe. He remained chest pain-free and was discharged 2 days later.

DISCUSSION

Coronary vasospasm is a condition caused by localized or diffuse vasoconstriction of an epicardial coronary artery, resulting in myocardial ischemia, ranging from rest angina to acute coronary syndrome. Coronary vasospasm in heart transplant is generally considered rare.[2] The largest single-center observation study on coronary vasospasm post-heart transplant demonstrated that 12 of 247 (4.9%) consecutive patients had vasospasm on routine surveillance coronary angiograms.[2] However, this observed prevalence may be inaccurate because patients in this study were asymptomatic and angiograms were done without provocative maneuvers. Previous case reports have described severe, symptomatic episodes of coronary vasospasm in heart transplant recipients, resulting in ventricular arrhythmias, high-degree atrioventricular block, and cardiac arrest.[3,4] Many patients do not report chest discomfort, perhaps related to denervation, although reinnervation occurs post-transplant to a variable degree and with a variable time course, as evidenced by the fact that some

FIGURE 1 Coronary Angiogram at Baseline and After Intracoronary Administration of Acetylcholine



(A) Baseline; (B) after intracoronary administration of 36 μg acetylcholine.

heart transplant recipients may report angina years after transplantation.[5]

The diagnostic criteria for vasospastic angina include ≥90% coronary artery diameter reduction, angina, and ischemic electrocardiogram changes with intracoronary acetylcholine administration.[1] Although the patient only met 2 of 3 criteria on functional coronary angiography, there was a clear association with classic chest discomfort correlating with vasospasm on angiogram. Early sensory reinnervation enabling cardiac-related chest pain is certainly possible in this patient given that an extensive work-up for other noncardiac causes of chest pain was negative. To date, there has been no previous case reports or studies describing this. This unique case illustrates the importance of maintaining a broad differential diagnosis in heart transplant recipients who present with chest discomfort early after transplantation and to not exclude cardiac sources from the list of potential etiologies.

Coronary vasospasm has been associated with accelerated coronary artery vasculopathy (CAV).[6] The pathogenic relationship and prognostic significance between coronary vasospasm and CAV is not well understood. In multiple case series, a small proportion of patients with post-transplant coronary vasospasm demonstrate subsequent epicardial coronary artery disease at a range of 1 to 3 years after diagnosis of vasospasm.[2,6,7] However, in these case series, assessment of CAV by maximal intimal thickness on intravascular ultrasound was not performed, which may have identified earlier signs of CAV.[8] Therefore, the true incidence of coronary vasospasm leading to CAV may be higher.

There is demonstrated benefit of proliferation signal inhibitors in attenuating the progression of CAV.[9,10] Whether this benefit extends to patients with coronary artery vasospasm is not established.

FOLLOW-UP

The patient had monthly follow-up in the heart transplant clinic per routine protocol. He was maintained on amlodipine with no recurrence of chest discomfort. He underwent surveillance coronary angiogram at 1-year post-transplant. On intravascular ultrasound, there was an increase in maximum intimal thickness of the mid LAD from 0.3 mm observed at 1-month post-transplant to 0.6 mm observed at 1-year post-transplant. Although the change in maximal intimal thickness was <0.5 mm, based on his history of coronary vasospasm and intimal thickness suggestive of endothelial cell dysfunction, he was switched from mycophenolate mofetil to sirolimus.

CONCLUSIONS

We present a case of chest pain in a heart transplant recipient only 5 months post-transplant that recurred at 8 months post-transplant with documented

coronary vasospasm on angiogram. This case illustrates an unusual presentation of coronary vasospasm with angina manifesting unexpectedly early after transplantation and emphasizes the difficulty in diagnosis; an angiogram was not performed until his second hospital stay 3 months after initial presentation. Lessons learned from this case include the importance of a broad differential diagnosis including cardiac causes of chest discomfort even early after transplantation, the role of provocative maneuvers to diagnose coronary vasospasm on angiography, and the need for vigilance for subsequent CAV in transplant recipients who present with vasospasm.

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