CASE PRESENTATION

Acute ST-segment elevation myocardial infarction in a heart transplant recipient

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Abstract: Introduction – Acute coronary syndromes are rare in heart transplant recipients. They are usually linked to cardiac allograft vasculopathy, one of the main complications of heart transplantation, characterized by early and rapidly progressing arteriosclerosis. Case presentation – We report the case of a 58-year-old female who underwent heart transplantation at the age of 44 years. The patient presented at the Emergency Department 24 h after the onset of unspecific symptoms (epigastric discomfort, fatigue, general weakness). A diagnosis of ST-segment elevation myocardial infarction was established based on the electrocardiogram and the increased levels of cardiac necrosis markers. Coronary angiogram revealed proximal occlusion of the right coronary artery, with no other atherosclerotic lesions. A drug-eluting stent was implanted, with good angiographic result. Post-angioplasty, the clinical course was uneventful. Conclusion – Acute myocardial infarction is a rare, but serious complication in heart transplant recipients. Symptoms can be misleading in this subgroup of patients and a careful evaluation of new symptoms should always be made. Although acute coronary syndromes are usually due to cardiac allograft vasculopathy, in our case, the presence of a single, focal coronary lesion of a proximal vessel at more than 14 years after heart transplant suggests typical atherosclerosis of the transplanted heart.

Keywords: heart transplant, cardiac allograft vasculopathy, STEMI


INTRODUCTION

Heart transplantation (HTx) is a life-saving procedure and the gold standard treatment for end-stage heart failure. However, the number of heart transplants is in decline, mainly due to the scarcity of donor organs1. Acute coronary syndromes (ACS) in HTx recipients are uncommon. Furthermore, due to cardiac denervation, initial presentation is usually atypical, with symptoms that may often be misleading2. Cardiac allograft vasculopathy (CAV), defined as early development of rapidly progressing coronary artery disease in the transplanted heart, represents one of the most important long-term complications of HTx and a major cause of morbidity and mortality in this subgroup of patients3. Allograft vasculopathy is characterized by an accelerated and diffuse process of arteriosclerosis, occurring in about 50% of patients at 5 years from transplantation4. Differentiating CAV from typical atherosclerosis can sometimes be difficult in clinical practice, although criteria have been published more than 10 years ago5.

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CASE REPORT

We present the case of a 58-year-old female who underwent HTx for end-stage heart failure secondary to ischemic dilated cardiomyopathy 14 years before. The patient first presented to her family physician for epigastric discomfort accompanied by intense fatigue, dizziness, and generalized weakness. She was prescribed antacids and no further investigations were performed. Due to persistence of symptoms, the patient presented the next day to the Emergency Department of our hospital, approximately 24 hours after symptoms onset.

Her medical history included arterial hypertension, obesity, and dyslipidemia. The patient was on long-term therapy with immunosuppressive agents (cyclosporine and mycophenolate mofetil), cotrimoxazole, calcium channel blocker, loop and mineralocorticoid antagonist diuretics, and a statin.

Physical examination showed a body mass index of 37.1 kg/m² and a heart rate of 70 beats per minute; her blood pressure was 110/90 mmHg; cardiac and pulmonary examinations were unremarkable. The electrocardiogram (Figure 1) revealed normal sinus rhythm with right bundle branch block (already known), ST-segment elevation in the inferior leads, alongside with pathological Q waves in the same territory, and depressed ST-segment in leads I and aVL, with inverted T waves in leads V3 to V6.

Cardiac necrosis biomarkers showed elevated troponin I (27.1 ng/ml), creatin kinase (3.000 IU/l), and creatin-kinase myocardial band (236 IU/l) levels. Trans-thoracic echocardiogram revealed hypokinesia of the left ventricular inferior wall, with a preserved left ventricular ejection fraction of 45%, grade I diastolic dysfunction, and moderate mitral regurgitation.

Based on these findings, the patient was diagnosed with acute inferior ST-segment elevation myocardial infarction (STEMI), and treated, according to current practice guidelines, with dual antiplatelet therapy (DAPT), low-weight molecular heparin, statin, and beta-blocker. Coronary angiogram revealed no atherosclerotic lesions of the left coronary artery (Figure 2 A and B), and proximal occlusion of the right coronary artery as culprit lesion (Figure 2 C). A drug-eluting stent was successfully implanted at the site of the lesion (Figure 2 D). The patient was discharged seven days later, after an uneventful evolution.

DISCUSSIONS

As the transplanted heart remains denervated over time, this subgroup of patients is lacking the typical symptoms of myocardial ischemia, making the diagnosis of ACS a real challenge. In a series of cases of acute myocardial infarction (AMI) in HTx recipients, only three out of 25 patients experienced typical chest or arm pain. The initial symptoms mainly consisted of dyspnea, fatigue, weakness, palpitations, dizziness, nausea, or diaphoresis. Only nine out of those 25 patients were admitted to hospital with an initial diagnosis of AMI, the rest being diagnosed either at the time of coronary angiography or at autopsy. Similarly, the initial presentation of our patient, with unspecific symptoms, was misleading and delayed the patient’s presentation to a percutaneous coronary intervention center. For an early detection of acute ischemia in this subgroup of patients, a high index of suspicion is therefore mandatory.

The underlying mechanism of STEMI in this patient may be related to either the initial atherosclerosis process, now affecting the transplanted heart, or to a late expression of CAV. Cardiac allograft vasculopathy has many similarities with native atherosclerotic disease; however, major differences have been shown to exist between the two conditions. From a pathophysiological point of view, CAV is initiated by intensive smooth muscle cells proliferation in the intima of the vessels and it may appear as early as 1 week or 2 weeks after transplantation, followed by accelerated progression of the disease. This process affects both the epicardial and the intramural vessels, but also the cardiac veins, resulting in diffuse vessel involvement. Meanwhile, typical atherosclerosis affects mainly the proximal epicardial coronary arteries. Also, whereas CAV typically

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Figure 1. Twelve-lead electrocardiogram showing normal sinus rhythm, with flat P waves and prolonged PQ interval (220 ms), ST-segment elevation in leads II, III, and aVF (arrows), pathological Q waves in the same territory, and complete right bundle branch block with secondary repolarization abnormalities.
for Heart and Lung Transplantation as surrogate marker for prognosis. Optical coherence tomography can diagnose and detect vulnerable plaques and complicated coronary lesions, whereas contrast echocardiography can assess the microcirculation by measuring the coronary flow reserve (CFR), reduced CFR being an early marker of CAV. Unfortunately, none of these techniques were used in our case, limiting our ability to distinguish with certainty between CAV and atherosclerosis. Evaluation of CAV biomarkers would also have been of interest. Indeed, several markers have been tested in this regard, from soluble interleukin-2 receptors, to cell type ratios, and, more recently, to microRNAs. However, none of these markers has imposed so far in clinical practice.

According to the recommendations of the International Society for Heart and Lung Transplantation, a diagnosis of CAV can be established based solely on coronary angiography and echocardiography parameters. In our patient, repeated coronary angiography and echocardiographic assessment at 1, 2, and 3 years post-HTx excluded the presence of de novo coronary

Figure 2. Coronary angiogram. Left coronary artery in right anterior oblique cranial view (A) and right anterior oblique caudal view (B). Complete occlusion of the right coronary artery (arrow) in left anterior oblique view (C), and opening of the artery after stent deployment in left anterior oblique view (D).
atherosclerosis and of CAV. The patient remained completely asymptomatic until the occurrence of the present STEMI, making it difficult to distinguish with certainty between typical coronary atherosclerosis and late-onset CAV. However, the finding of single-vessel involvement, the presence of a focal lesion in only one of the major epicardial coronary arteries, together with the absence of impaired left ventricular ejection fraction and of a restrictive profile of the left ventricular diastolic function, may be interpreted as signs of systemic atherosclerotic disease rather than CAV, as previously suggested by Fazio et al. However, given the scarcity of such cases, it remains difficult to draw a firm conclusion. Adequate differentiation between typical atherosclerosis and CAV may have important therapeutic impact, given that although both CAV and de novo atherosclerosis could benefit from percutaneous coronary interventions or coronary artery bypass-graft, the most effective therapy in severe CAV cases remains cardiac re-transplantation.

According to the current guidelines regarding the management of patients presenting with STEMI, DAPT will be continued for up to 12 months in our patient. The role of aspirin after heart transplantation has been controversial, recent data suggesting it may reduce the risk of CAV and mortality in HTx patients. In our case, considering the presence of an ACS in a heart transplant recipient, aspirin will be continued lifelong. In addition to aspirin, statins are also well known to influence short-term and long-term prognosis in this subset of patients by reducing cholesterol levels, improving endothelial dysfunction, and having anti-inflammatory activity; accordingly, lifelong statin therapy was also prescribed. Although our patient can be considered at very high risk of complications, there are no data so far to recommend more aggressive therapies, such as lifelong DAPT or association of DAPT with oral anticoagulation.

Adequate treatment of AMI in our patient will also have to be followed by a very close follow-up, given that late development of an atherosclerotic lesion in an HTx recipient appears to trigger rapid atherosclerosis progression.

**Conclusion:** Acute myocardial infarction is a rare, but serious complication in HTx recipients. Symptoms can be misleading in this subgroup of patients; the onset of any possibly cardiac-related new symptoms should lead to careful examination and exclusion of ischemic events. Although ACS are usually due to CAV, in our case, the presence of a single, focal coronary lesion of a proximal vessel, at more than 14 years after HTx, suggests typical atherosclerosis of the transplanted heart.

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**References**


