

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

Rezumat: **Introducere** – Sindroamele coronariene acute sunt rare la pacienții cu transplant cardiac, fiind datorate în principal vasculopatiei de allograft, una dintre principalele complicații post-transplant cardiac, caracterizate prin apariția precoce și evoluția rapidă a aterosclerozei. **Prezentare de caz** – Prezentăm cazul unei paciente de 58 de ani, care a beneficiat de transplant cardiac la vârsta de 44 de ani. Pacienta s-a prezentat la serviciul de urgență la 24 de ore de la debutul unor simptome nespecifice (disconfort epigastric, oboseală, astenie generalizată). Pe baza electrocardiogramei și a nivelurilor crescute ale markerilor de necroză miocardică s-a stabilit diagnosticul de infarct miocardic acut inferior cu supradenivelare de segment ST. Coronarografia a evidențiat ocluzia proximală a arterei coronare drepte, fără alte leziuni semnificative angiografice. S-a efectuat angioplastie cu implantare de stent farmacologic activ, cu rezultat angiografic bun. Evoluția post-angioplastie a fost favorabilă. **Concluzii** – Infarctul miocardic acut reprezintă o complicație rară, dar severă la pacienții cu transplant cardiac. Simptomele deseori atipice impun o evaluare atentă. Deși de obicei sindroamele coronariene acute se datorează vasculopatiei de allograft, în cazul nostru, prezența unei singure leziuni coronariene focale, cu localizare proximală, apărute la 14 ani post-transplant, sugerează mai degrabă reaparitia aterosclerozei clasice la nivelul cordului transplantat.

Cuvinte cheie: transplant cardiac, vasculopatie cardiacă de allograft, 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 ven-

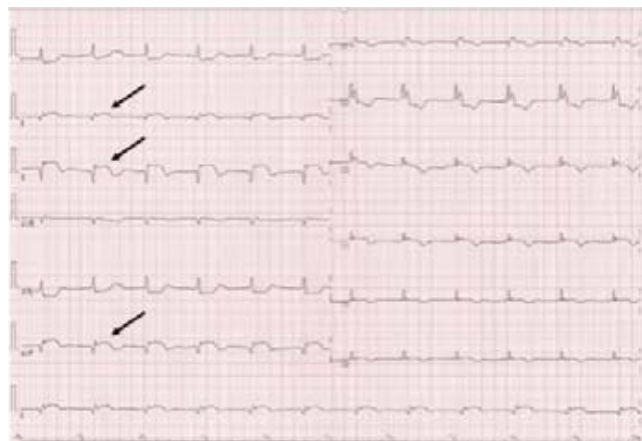


Figure 1. Twelve-lead electrocardiogram showing normal sinus rhythm, with flat P waves and prolonged PQ interval (220 ms), ST-segment elevation in leads II, III, and aVF (arrows), pathological Q waves in the same territory, and complete right bundle branch block with secondary repolarization abnormalities.

tricular 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 pain⁶. 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

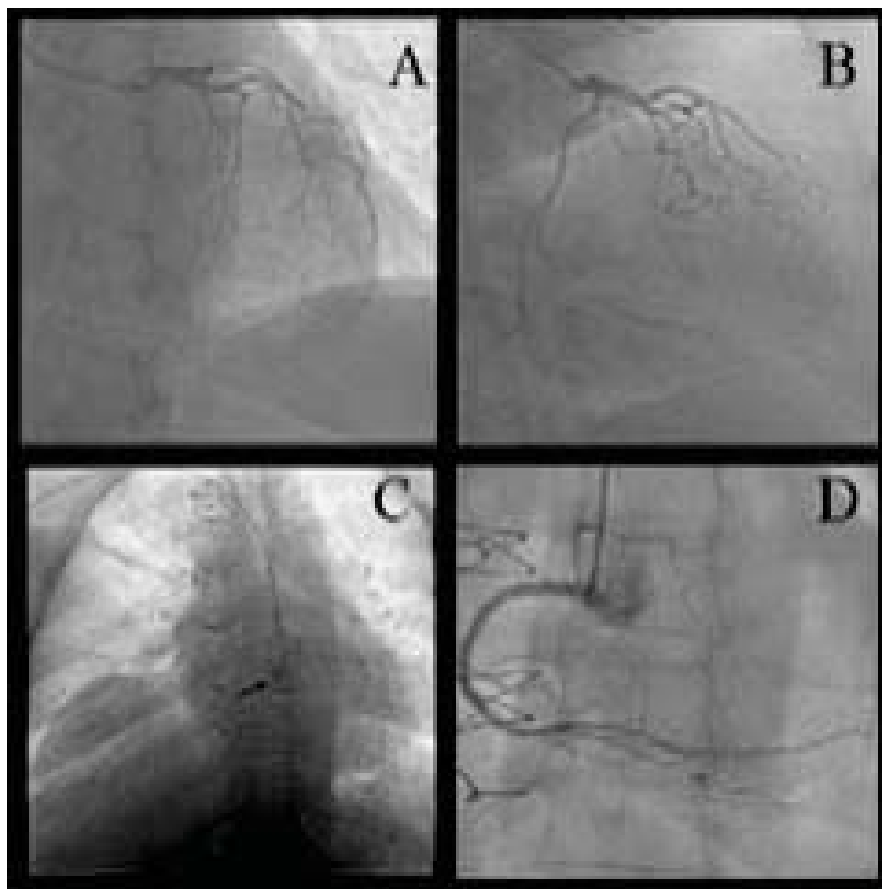


Figure 2. Coronary angiogram. Left coronary artery in right anterior oblique cranial view (A) and right anterior oblique caudal view (B). Complete occlusion of the right coronary artery (arrow) in left anterior oblique view (C), and opening of the artery after stent deployment in left anterior oblique view (D).

consists of concentric and diffuse intimal thickening, leading to extended vessel narrowing^{7,8}, typical atherosclerosis usually causes multiple, focal, eccentric lesions of the intima. Despite their different manifestations, typical atherosclerosis and CAV share common risk factors. The onset and development of both CAV and typical atherosclerosis are triggered by factors such as hyperlipidemia, diabetes mellitus, arterial hypertension, infections, inflammation, and smoking. On the other hand, factors such as ischemia/reperfusion graft injury, cytomegalovirus infection, and HLA-directed antibodies were shown to interfere only with CAV progression^{9,10}.

In clinical practice, the diagnosis of CAV relies on both coronary angiography (i.e., diffuse lesions of the epicardial coronary arteries) and echocardiography (impaired left ventricular ejection fraction, restrictive profile of the left ventricular diastolic function) data^{11,12}. Other modern imaging techniques have also proved useful for CAV diagnosis. Intravascular ultrasound can detect and quantify the early signs of intimal thickening^{13,14}, being proposed by the International Society

for Heart and Lung Transplantation as surrogate marker for prognosis. Optical coherence tomography can diagnose and detect vulnerable plaques and complicated coronary lesions¹⁵, whereas contrast echocardiography can assess the microcirculation by measuring the coronary flow reserve (CFR), reduced CFR being an early marker of CAV¹⁶. 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 receptors¹⁷, to cell type ratios¹⁸, and, more recently, to microRNAs¹⁹. 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 parameters⁵. In our patient, repeated coronary angiography and echocardiographic assessment at 1, 2, and 3 years post-HTx excluded the presence of *de novo* coronary

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 al²⁰. 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^{21,22}, the most effective therapy in severe CAV cases remains cardiac re-transplantation²³.

According to the current guidelines regarding the management of patients presenting with STEMI²⁴, DAPT will be continued for up to 12 months in our patient. The role of aspirin after heart transplantation has been controversial²⁵, recent data suggesting it may reduce the risk of CAV and mortality in HTx patients²⁶. 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 activity²⁷; 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 progression²⁸.

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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Conflicts of interest: none declared.

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