COMUNICACIÓN BREVE

Left main coronary artery stenosis treatment with two paclitaxel-eluting stents in a patient with cardiac allograft vasculopathy

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Summary

Cardiac transplantation is a well defined therapy for end stage heart failure. After the first year of transplantation, allograft coronary artery disease (ACAD) is the second main cause of death. The ACAD is defined as a diffuse process affecting the entire length of epicardial vessels. Once ACAD has been established, treatments such as coronary angioplasty, coronary stenting, and coronary bypass are performed. We present a case of successful stenting of the left main coronary artery (LMCA) in a patient with ACAD. The patient's medical history was significant for heart transplantation due to ischemic heart failure. Four years after transplantation the patient was admitted again due to sudden worsening of New York Heart Association functional class and extreme fatigue. Coronary angiogram showed a severe stenosis in the proximal segment of the LMCA; we performed stenting with a paclitaxel-eluting stent (PES). Six months after the procedure, the patient had an elective angiogram, where we discovered a new severe occlusion distally to the former stent; a second PES was implanted. Fourteen months after the

Resumen

TRATAMIENTO DE UNA ESTENOSIS DEL TRONCO DE LA CORONARIA IZQUIERDA CON DOS STENTS LIBERADORES DE PACLITAXEL EN UN PACIENTE CON VASCULOPATÍA CORONARIA POSTRASPLANTE

El trasplante cardíaco es uno de los principales tratamientos para la insuficiencia cardíaca avanzada. Una de las principales complicaciones de este procedimiento es la vasculopatía postrasplante (VCPT), cuyas opciones terapéuticas son la angioplastía y/o implantación de stent, y la cirugía de revascularización. En este reporte presentamos el caso de un paciente con VCPT en el tronco de la coronaria izquierda (TCI) tratado con implantación de stent. El motivo del trasplante cardíaco fue insuficiencia cardíaca avanzada de etiología isquémica. Cuatro años posteriores al trasplante, el paciente fue reingresado debido a empeoramiento de su clase funcional y fatiga extrema. La angiografía coronaria mostró una estenosis severa en el segmento proximal del TCI, por lo que procedimos a implantar un stent liberador de paclitaxel (SLP). Seis meses después, se realizó una angiogra-

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second stenting, a new elective angiogram was performed without evidence of in-stent restenosis. After a 8-year follow-up since transplantation, the patient is free from dyspnea, angina, and adverse cardiovascular events. Our report suggests the efficacy of PES as ACAD treatment of the unprotected LMCA.
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fía de control demostrándose una nueva oclusión severa inmediatamente distal al primer stent implantado, por lo que se decidió colocar un segundo SLP. Catorce meses después del segundo intervencionismo se realizó una nueva angiografía selectiva, la cual se reportó sin evidencia de reestenosis intrastent. Después de 7 años de seguimiento, el paciente se reporta sin disnea, angina o eventos cardiovasculares adversos. Nuestro reporte sugiere que la utilización del SLP puede ser efectiva en el tratamiento de la VCPT en el TCI no protegido.

Introduction

Cardiac transplantation is a well defined therapy for end stage heart failure. After transplantation, median survival is from 9.6 to 12 years.[1] The main causes of death in the first year after transplantations are infection, rejection, and graft failure. After the first year of transplantation, allograft coronary artery disease (ACAD) is the second main cause of death, just after malignancy.[2] In a registry from the International Society of Heart and Lung Transplantation (ISHLT), ACAD is reported in only 2.4% of survivors at 1 year but in 8.9% at 5 years (A).[1]

The ACAD is defined as a diffuse process affecting the entire length of epicardial vessels, including intramyocardial branches. Histological studies reveal a lesion characterized by concentric intimal proliferation, with general sparing of the elastic lamina.[3] This process is different from classical coronary artery disease (CAD), which tends to be focal and eccentric with marked involvement of the elastic lamina. In grafts with longer survival, there may be both focal and atheromatous disease as well as diffuse concentric intimal thickening.[4]

When ACAD has been established, treatments such as coronary angioplasty, coronary stenting, and coronary bypass offer only symptomatic relief and palliative care. The only effective treatment is to repeat transplantation, which is a main subject of ethical and moral discussion, especially with the shortage of donors.[5]

Percutaneous coronary intervention (PCI) of the unprotected left main coronary artery (LMCA) is currently not recommended as a routine procedure based on the history of inferior outcomes of left main (LM) percutaneous transluminal coronary angioplasty and bare metal stenting.[6] Instead, surgical revascularization (coronary artery bypass grafting [CABG]) is considered to be the gold standard. There is renewed interest in LM-PCI because improved outcomes of PCI utilizing drug eluting stents (DES) in multiple randomized trials. Several single-center non-randomized registries have evaluated the role of DES for LMCA-PCI. Data suggest a low mortality and target vessel failure of ostial LM or midshaft lesions in contrast to bifurcation lesions.

Case report

A 49 year-old man was admitted because of sudden worsening of New York Heart Association (NYHA) functional class and extreme fatigue. The patient's medical history was significant for orthotopic heart transplantation four years earlier (September 2000) as treatment for ischemic heart failure due to massive myocardial infarction, DDD pacemaker implantation (August 2002) due to intermittent sinusal pauses and bradycardia, as well as hypertriglyceridemia and smoking. The patient did not have any history of severe graft rejection, angina or evidence of myocardial ischemia in the routine postransplant studies (99mTc-MIBI stress-rest myocardial perfusion scintigraphy, exercise stress test, radionuclide ventriculography, and echocardiography). Home medications were tacrolimus, mycophenolate mofetil, prednisone, pravastatin, amlodipine and isosorbide mononitrate. Complete blood count and a metabolic panel, including normal serial creatinine concentrations, were within normal limits. Low density lipoprotein ranged between 83.8 mg/dL, high

density lipoprotein between 50 mg/dL, and triglyceride concentrations between 216 mg/dL over the preceding two years.

Once admitted, an echocardiogram showed a significant deteriorated systolic function (the left ventricular ejection fraction was 45%). Coronary angiogram showed only a significant (70%) focal coronary occlusion in the proximal segment of the left main stem. During the procedure, an endomyocardial biopsy was performed, which demonstrated a grade III graft rejection of the ISLHT (International Society for Heart & Lung Transplantation) classification. An intraaortic balloon counterpulsation was implanted and treatment was initiated with basiliximab, and the dose of tacrolimus, mycophenolate mofetil and prednisone were adjusted. After three weeks of treatment another endomyocardial biopsy showed absence of rejection.

Finally, an angioplasty was attempted in the LMCA. Clopidogrel (300 mg) was administrated in the catheterization laboratory. The left main coronary artery was cannulated with a 8-French left guide catheter with side holes and the lesion was crossed with a 0.014-inch Hi-Torque Floppy coronary guidewire. The lesion was dilated twice with 3.0 x 20 mm Maverick balloon at 18 atm during four seconds. A 3.5 x 8 mm Taxus stent was deployed in the left main stem at 18 atm during thirteen seconds with good results. There was no residual stenosis of evidence of complications. The patient left the hospital the following day. One year of treatment with clopidogrel was recommended. On clinical follow-up after the angioplasty an echocardiogram showed improvement of the left ventricular ejection fraction and the patient reported a marked enhancement in his ability to perform sustained exercise without suffering from shortness of breath (NYHA functional class I) and angina *(Fig. 1)*.

Six months after the interventional procedure, the patient underwent an elective follow-up angiogram. It showed a new 70% focal occlusion immediately distal to the former stent placed, in the distal segment of the LMCA. Similar technique as described in the first angioplasty was performed but in this case a 3.5 x 12 mm Taxus stent was placed covering the distal LMCA and proximal left anterior descending coronary artery *(Fig. 2)*.

Fourteen months after the second stenting a new elective angiogram was performed. It showed patent stents in the LMCA, without evidence of other significant occlusions *(Fig. 3)*. After a 7-year follow-up since transplantation, the patient is free from dyspnea, angina and major adverse cardiovascular events and presents a conserved left ventricular ejection fraction.

Discussion

ACAD represents a main obstacle to long-term survival after heart transplantation. There is a linear and steady risk of developing ACAD detected on angiograms after the first year from transplantation, so that by the fifth year, more than 50% of transplanted recipients will present some disease.[7] Ahead of five years, the risk of presenting angiographically noticeable severe ACAD increases proportionally, illustrated by the fact that nine years after transplantation 29% of patients will have detectable disease.[8] About 25% of all deaths between the first and tenth year after transplantation will be due to ACAD.[7] Once three-vessel or severe ACAD is developed, the risk of death or retransplantation is extremely high within one year after diagnosis.[9]
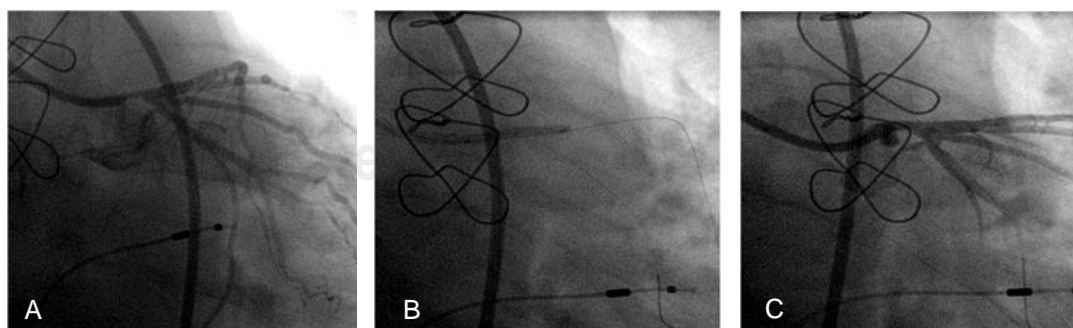
Fig. 1. Coronary angiography showing a 70% stenosis on the left main coronary artery arising from the ostium (A). Implantation of a 3 x 8 mm paclitaxel-eluting stent (B). Optimal angiographic result immediately after stenting (C).
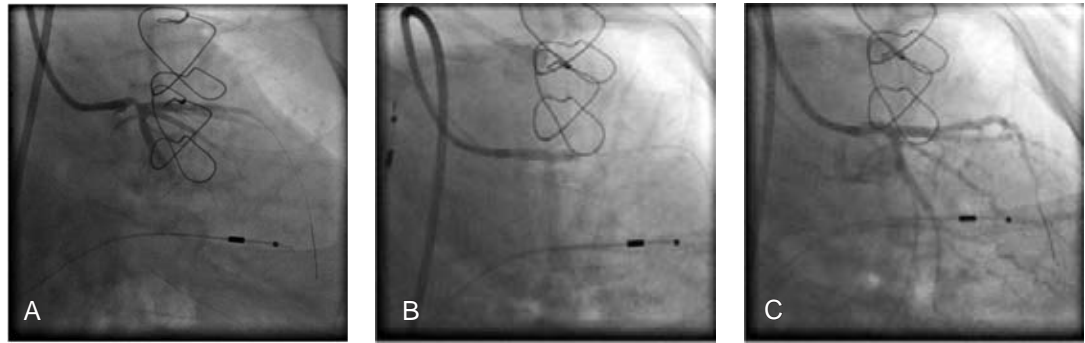
Fig. 2. Coronary angiography showing a 70% stenosis on the left main coronary artery just distal to the first stent implanted and obstructing proximal (A). Implantation of a 3 x 12 mm paclitaxel-eluting stent (B). Optimal angiographic result immediately after stenting (C).
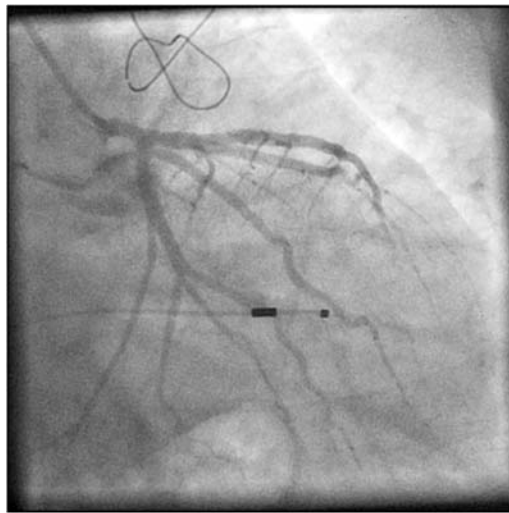
Fig. 3. Left anterior oblique projection showing the widely opened left main coronary artery after 14 months.

The diagnosis of ACAD is challenging. Traditional symptoms of angina are often absent and patients have a tendency to present with heart failure, just as we show in the present report. Otherwise, ACAD is mainly diagnosed on angiography or intravascular ultrasound (IVUS), if routinely performed; as the former usually underdiagnose ACAD, a classification system was created by Stanford University that distinguishes ACAD going from typical atherosclesis to concentric arterial occlusion.[10] Angiograms should be interpreted consecutively as new concentric lesions may be missed on one-time angiograms analysis. The IVUS, however, has the benefit of picturing the entire arterial wall and is more sensitive and specific. The Stanford group

also proposed a classification system.[11] A study by Kapadia *et al* established that all three-vessels imaging with IVUS revealed up to two times the amount of ACA at 1 year (58% *versus* 27%) and this trend persisted for three years.[12]

Before transplantation the medical team should focus on preventing endothelial injury and brain death, reducing cold ischemic time, and improving myocardial preservation during storage and transportation.[13] Following transplantation, the focus should be on prevention of ACAD by attenuation of adverse nonimmunological and immunological reaction. Modification of traditional risk factors such as diabetes, dyslipidemia, hypertension, and smoking is a key factor in the prevention of endothelial dysfunction and thus development of ACAD.[14]

Certain therapies for ACAD have been shown to slow the progression of the disease, and therefore they tend to decrease mortality. Drugs such as 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors and calcium-channel blockers have some protective effect, but they do not eliminate entirely the problem.[3] Newer immunosuppressants such as sirolimus and everolimus can be useful.[15] The CABG has been associated with a high peri-operative mortality of up to 30%.[16] The ineffective medical treatment and the limited suitability of CABG and retransplantation have motivated interest in PCI for the subset of heart transplant recipients presenting with allograft vasculopathy in proximal segments.

There is some evidence that supports PCI as a therapy in ACAD. In 1995 Halle *et al*,[16] reported a 55% restenosis incidence at 8 ± 5 months after angioplasty and angiographic distal arteri-

opathy adversely affected allograft survival. In 1998 Musci *et al*[17] studied 46 patients who underwent 76 angioplasties at a mean of 50 ± 30 months; they reported 96% primary success rate and angiographic restenosis occurred in 42% with no procedure-related death. In 2000 Schnetzler *et al*[18] reported their experience in 29 transplanted patients with 53 coronary sites dilated; they described a primary success rate of 94.3% with a 32.5% stenosis rate at 1.27 ± 1.2 years, and they did not found any factor predictive for restenosis in this population; although they informed about 2 patients with a LMCA stenosis who were treated with PCI, one of them had restenosis and underwent to CABG.

ACAD is one of the most insidious complications limiting long-term survival of transplanted patients. The option of using stents eluting different drugs might help in the treatment of this feared condition. Most reports suggest a low major adverse cardiac events rate for PCI in ostial or mid-shaft LMCA disease, while data are more heterogeneous for PCI in distal LM disease involving the bifurcation.[19,20] Stent implantation is technically viable and is related to an optimal early outcome. The real problem is the unknown risk of restenosis in these patients with often ominous clinical presentation. Routine follow up angiography comes forward to be necessary for the opportune diagnosis of restenosis. To the best of our knowledge, this is the first reported case of successful double paclitaxel stenting for LMCA stenosis in a patient with ACAD. The effect of drug eluting stents on LMCA occlusions needs further investigation, as this treatment modality may be an effective alternative for this very high risk group of patients.

Acknowledgements

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