CASE REPORT

Heart Transplantation and Bone Marrow Transplantation in a Patient with AL Amyloidosis and Refractory Heart Failure

CÉSAR BELZITI[MTSAC, 1], RODRIGO BAGNATI[1], CAROLINA TORRES BIANQUI[1], JORGE ARBELBIDE[2], ELSA NUCIFORA[2], ALBERTO DOMENECH[MTSAC, 3], RICARDO MARENCHINO[3], NORBERTO VULCANO[MTSAC, 1], ARTURO CAGIDE[MTSAC, 1]

Received: 05/22/2009
Accepted: 06/03/2009

Address for reprints:
Dr. César A. Belziti
Servicio de Cardiología
Hospital Italiano de
Buenos Aires
Gascón 450
(C1181ACH) CABA

SUMMARY

Primary amyloidosis is a systemic infiltrative disease that compromises the heart and represents an important cause of restrictive cardiomyopathy.
We describe a 35-year old man with advanced heart failure secondary to an infiltrative cardiomyopathy with amyloid deposition. A plasma cell neoplasm was also diagnosed. The patient evolved with rapid progression of symptoms and deterioration of ventricular function, and did not tolerate the adequate therapy due to the hematological disease. For this reason, he underwent heart transplantation followed by autologous bone marrow transplantation; no complications were reported. This is the first case of heart transplantation followed by bone marrow transplantation reported in our country for the treatment of cardiac amyloidosis.

REV ARGENT CARDIOL 2009;77;309-311

Key words > Heart Transplantation - Bone Marrow Transplantation - Amyloidosis - Heart Failure

Abbreviations >

BNP	B-type natriuretic peptide	**ECG**	Electrocardiogram
FC	Functional class	**LV**	Left ventricle

BACKGROUND

Primary amyloidosis is a systemic infiltrative disease that compromises the heart and represents an important cause of restrictive cardiomyopathy. Cardiac involvement occurs in up to 50% of cases of systemic AL amyloidosis (deposition of immunoglobulin light chain fragments); isolated cardiac impairment is rare. Right-sided heart failure is the most frequent clinical presentation; however, left ventricular diastolic or systolic dysfunction with low cardiac output may also be present. Syncope is another clinical manifestation and is related to multiple factors; conduction system disturbances are also frequent. Mean survival after diagnosis of cardiac amyloidosis is 1.1 years, and it decreases to 6-9 months once heart failure has developed. (1,2) In this setting, heart transplantation may improve the survival. (1, 3)

CASE REPORT

This is the first case of heart transplantation followed by bone marrow transplantation reported in our country for the treatment of cardiac amyloidosis secondary to multiple myeloma.

A 35-year old man was transferred to our hospital on June 3, 2008, due to decompensated heart failure. He had neither cardiovascular risk factors nor personal history of cardiovascular diseases.

Until the end of 2007, he used to practice sports every day without problems. Thereafter, he started with dyspnea in NYHA functional class (FC) II that rapidly progressed to FC IV.

He was hospitalized with signs of volume overload and was treated with intravenous diuretics. The electrocardiogram showed sinus rhythm, right QRS axis deviation (+120º), poor R wave progression from V1 to V3 and absence of R waves in the inferior wall. There were no signs of acute ischemia. Doppler echocardiography showed preserved left ventricular systolic function, concentric left ventricular hypertrophy, restrictive left ventricular filling pattern, right and left atrial enlargement and mild mitral regurgitation.

The patient underwent coronary angiography which showed absence of significant lesions in the coronary arteries. He was transferred to the Hospital Italiano de Buenos Aires for further evaluation with a diagnosis of congestive heart failure secondary to non ischemic cardiomyopathy.

Hospital Italiano de Buenos Aires
[MTSAC] Full Member of the Argentine Society of Cardiology
[1] Department of Cardiology
[2] Department of Hematology
[3]Departement of Cardiovascular Surgery

At admission, the patient had signs of heart failure with hypotension (90/60 mm Hg); no other signs of low cardiac output were detected. The admission electrocardiogram was similar to the previous records. The results of the lab tests revealed discrete anemia and renal dysfunction: hematocrit 36%, hemoglobin level 12.5 g/dl, creatinine clearance 61 ml/min/1.73 m^2. Troponin T level was 1.2 ng/ml (reference value < 0.04 ng/ml) and BNP was 2461 pg/ml. Chest X-ray showed cardiomegaly, a straight main pulmonary artery border and pulmonary venous congestion. A second echocardiogram confirmed the previous results: preserved left ventricular function, left ventricular hypertrophy (interventricular septum thickness: 1.78 cm; posterior wall thickness: 1.55 mm), left and right atrial enlargement (left atrial anteroposterior diameter: 5.2 cm) and a restrictive left ventricular filling pattern. Myocardial hyperrefractile appearance was consistent with cardiac amyloidosis (Figure 1). Gadolinium-enhanced cardiac magnetic resonance imaging showed the distinctive feature of cardiac amyloidosis. An endomyocardial biopsy confirmed the diagnosis (Figures 2 and 3).

Immunoelectrophoresis identified lambda light chains in blood and urine, confirming cardiac amyloidosis secondary to lambda light-chain deposition. A plasma cell infiltration > 25% in the bone marrow suggested plasma cell neoplasm.

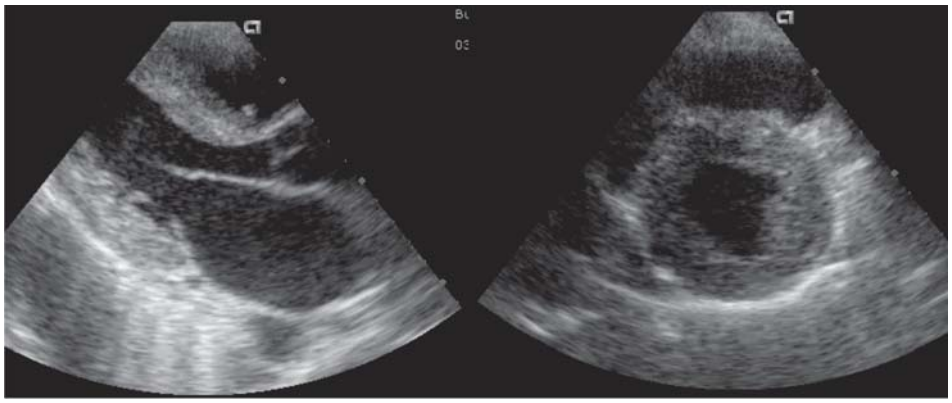

Fig. 1. Admission echocardiogram. Pronounced hypertrophy, sparkling-granular appearance of the myocardium, normal left ventricular diameters and left atrial enlargement are observed.

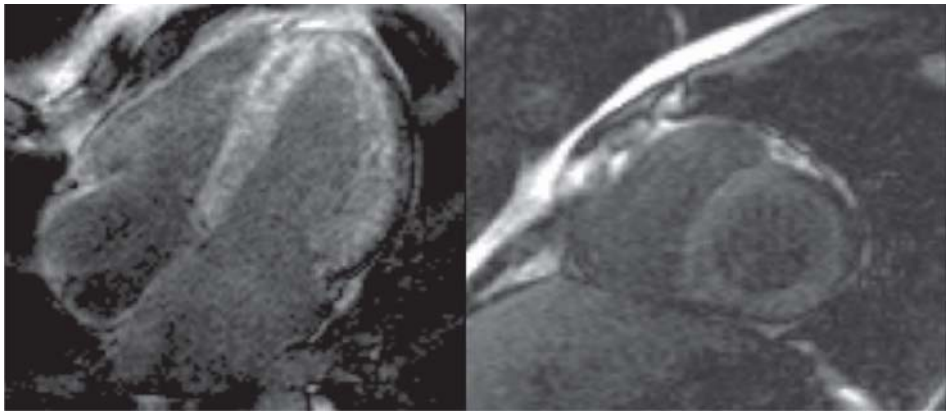

Fig. 2. Cardiac magnetic resonance imaging. Late gadolinium enhancement image shows diffuse subendocardial enhancement and transmural enhancement at the level of the septum. When normal myocardium signal is suppressed, blood pool signal decreases. These findings are consistent with cardiac amyloidosis.

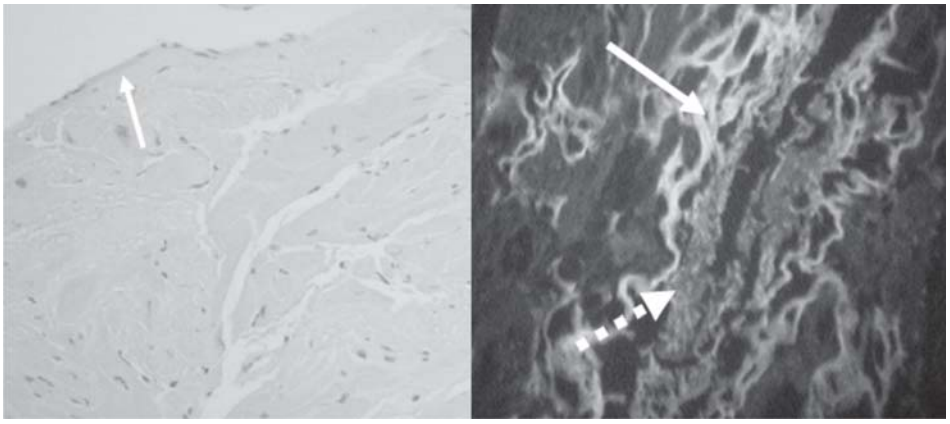

Fig. 3. *Left*: Endomyocardial biopsy; hematoxylin and eosin stain. Typical amyloid deposition in the heart is seen as eosinophilic amorphous substance in the intercellular space, predominantly at the subendocardium *(arrow.)* *Right*: Thioflavin stain of the same tissue specimen. Note the pericellular deposition of fluorescent material *(arrow)* and the compromise of the vascular wall interstice *(dotted arrow).*

Therapy with a combination of bortezomib, cyclofosfamide and dexamethasone was initiated; at the beginning of the second cycle light chains in urine were no longer detected. Stem cells were cryopreserved for bone marrow transplantation. Therapy was discontinued due to hypotension and syncope during treatment.

The patient evolved with progressive deterioration in left ventricular function and refractory heart failure, and was included in the heart transplant waiting list.

He was rehospitalized with signs of low cardiac output four months after the first admission. He required inotropic drugs and continuous intravenous infusion of diuretics; an intraaortic balloon pump was implanted. On November 11, 2008, he underwent heart transplantation. He did not present any complications and was discharged on November 20, 2008. The patient evolved with favorable outcomes and his functional capacity was within normal ranges. Bone marrow aspiration and serum and urine immunofixation tests were normal. A slight increase in blood levels of free lambda light chains (33.5 mg/L; reference value: 5.7-26.3 mg/L) after chemotherapy before heart transplantation indicated active amyloidosis.

Cardiac magnetic resonance imaging did not demonstrate new amyoloid infiltration of the graft. In consequence, the patient underwent bone marrow transplantation for his hematologic condition.

After an infusion of 200 mg/m^2/dose of melphalan, autologous bone marrow transplantation was performed on March 19, 2009. Head and torso mucositis and folliculitis secondary to therapy with corticosteroirds were the only adverse events. One year after the diagnosis, the patient is currently followed-up at the outpatient clinic; endomyocardial biopsies show absence of amyloid deposits; serum free lambda light chains are within normal ranges and his clinical status is very good.

DISCUSSION

Infiltrative cardiomyopathy due to amyloid deposition has an adverse prognosis; survival rate is < 1 year in untreated patients. Heart transplantation has not been routinely used in patients with primary and secondary amyloidosis due to extracardiac amyloid deposits and to the possibility of recurrences in the transplanted heart with a poor long-term prognosis. (1-4)

However, during the last years some studies have reported promising results with high-dose melphalan in AL amyloidosis associated with bone marrow autologous transplantation. This therapy is useful to suppress and eradicate the plasma cell clone; complete remission is achieved in up to 50% of cases. Yet, this therapy has a high mortality rate (14-30%), especially in patients with advanced heart failure who cannot put up with this dosage regime. In these cases, when systemic involvement is limited, heart transplantation may constitute a therapeutic option for heart failure; thereafter chemotherapy and bone marrow transplantation may be tolerated, (5) The results achieved with this strategy are promising, with improved short and long-term prognosis. (6-7)

RESUMEN

Heart Transplantation and Bone Marrow Transplantation in a Patient with AL Amyloidosis and Refractory Heart Failure

La amiloidosis es una enfermedad infiltrativa sistémica que compromete al corazón y representa una causa importante de miocardiopatía restrictiva.
Se describe el caso de un paciente masculino de 35 años con insuficiencia cardíaca avanzada secundaria a miocardiopatía infiltrativa por depósito amiloide. Durante su evaluación se realizó diagnóstico de neoplasia de células plasmáticas. Debido a la rápida progresión de los síntomas, el deterioro de la función ventricular y la incapacidad para tolerar el tratamiento adecuado para su enfermedad hematológica, se realizó trasplante cardíaco seguido de trasplante autólogo de médula ósea sin complicaciones. La presentación de este caso constituye la primera comunicación en nuestro país de trasplante cardíaco seguido de trasplante de médula ósea como tratamiento de la amiloidosis cardíaca.

Palabras clave > Trasplante de corazón - Trasplante de médula ósea - Amiloidosis - Insuficiencia cardíaca

BIBLIOGRAPHY

1. Hassan W, Al-Sergani H, Mourad W, Tabbaa R. Amyloid heart disease. New frontiers and insights in pathophysiology, diagnosis, and management. Tex Heart Inst J 2005;32:178-84.

2. Marin JE, Duque M, Medina LE, Uribe W, Velásquez JE. Cardiac amyloidosis. Rev Col Cardiol 2005;11:389-96.

3. Dubrey SW, Burke MM, Hawkins PN, Banner NR. Cardiac transplantation for amyloid heart disease: the United Kingdom experience. J Heart Lung Transplant 2004;23:1142-53.

4. Dubrey SW, Burke MM, Khaghani A, Hawkins PN, Yacoub MH, Banner NR. Long term results of heart transplantation in patients with amyloid heart disease. Heart 2001;85:202-7.

5. Perz JB, Kristen AV, Rahemtulla A, Parameshwar J, Sack FU, Apperley JF, et al. Long-term survival in a patient with AL amyloidosis after cardiac transplantation followed by autologous stem cell transplantation. Clin Res Cardiol 2006;95:671-4.

6. Hosenpud JD, Uretsky BF, Griffith BP, O'Connell JB, Olivari MT, Valantine HA. Successful intermediate-term outcome for patients with cardiac amyloidosis undergoing heart transplantation: results of a multicenter survey. J Heart Transplant 1990;9:346-50.

7. Maurer MS, Raina A, Hesdorffer C, Bijou R, Colombo P, Deng M, et al. Cardiac transplantation using extended-donor criteria organs for systemic amyloidosis complicated by heart failure. Transplantation 2007;83:539-45.