Cardiac Amyloidosis: The Importance of a Multidisciplinary Approach

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BRIEF REPORT

Cardiac amyloidosis is associated with the interstitial deposition of abnormal protein in the myocardium, which can lead to a form of restrictive cardiomyopathy with a poor prognosis. This protein can have a number of different origins, which give rise to various subtypes of amyloidosis that have different prognoses and that require different therapeutic approaches. Drugs commonly used in heart failure have little effect in amyloidosis and the use of heart transplantation is controversial because amyloidosis is a multi-organ disease and because there is a possibility of disease recurrence in the graft.

The use of new techniques to identify the specific amyloidosis subtype, the emergence of novel ways of preventing or decreasing amyloid production, the ability to monitor responses to therapy and, above all, the introduction of multidisciplinary teams that can implement a combination of therapies, including multiple organ transplantation, have contributed to a substantial improvement in the prognosis of this disease.

Key words: Cardiac amyloidosis. Restrictive cardiomyopathy. Heart transplantation.

INTRODUCTION

Cardiac amyloidosis (CA) is caused by deposition of an insoluble protein material, known as amyloid substance, in the cardiac interstitium. This abnormal protein can have different origins and molecular compositions, thus giving rise to different types of amyloidosis. CA can be part of a systemic disease with involvement of other organs, or, more rarely, affect only the heart. The condition usually presents as a restrictive cardiomyopathy that leads to death from heart failure in most patients. The indication for cardiac transplantation (CTx) is controversial because of poor post-transplantation survival related to multiorgan involvement and the probability of recurrence in the transplanted organ. Fortunately, recent advances in the management of CA have improved the life expectancy of affected patients.

METHODS

Three patients with CA evaluated in our unit during 2005 to 2007 are presented. All underwent combined treatments that included CTx.
restrictive, infiltrative cardiomyopathy (Figure 1). Endomyocardial biopsy (EMB) confirmed the suspected diagnosis of CA, and bone marrow biopsy (BMB) demonstrated 8% monoclonal plasma cells, confirming the diagnosis of primary (AL) amyloidosis. Additional examinations excluded significant involvement of other organs.

Because of the patient’s rapid hemodynamic deterioration, he required intra-aortic balloon...
failure; hence he was referred to our hospital for CTx assessment. The clinical signs and symptoms were not typical of primary amyloidosis because of the slow evolution, absence of a monoclonal peak in blood and urine, and a normal BMB, which raised the suspicion of another diagnosis. Scintigraphy with technetium-99m dicarboxypropane diphosphonate (99mTc-DPD) demonstrated radioisotope uptake in the myocardium, and immunohistochemistry of EMB specimens showed transthyretin deposition. Genetic studies disclosed a heterozygous mutation (Glu89Lys) in the transthyretin gene, which established the diagnosis of familial amyloidogenic transthyretin (ATTR) amyloidosis (neuropathic amyloidosis). The evaluation included an electroneurogram, which evidenced moderate sensory-motor polyneuropathy.

Because of the patient’s poor clinical evolution, he was included on the waiting list for a CTx, which was ultimately carried out without complications (Figure 2). Six months later he was placed on the liver transplantation (LTx) waiting list, where he remained for 1.5 years, during which time the EMB showed no amyloid and his neuropathy progressed slowly, without causing significant disability. Three years following CTx and 1 year after LTx, at the time of writing, the patient is able to maintain a normal lifestyle.

Patient 2

A 52-year-old man with no family history of interest had a background of bilateral carpal tunnel syndrome and pacemaker implantation 4 years previously due to atrial fibrillation and a slow ventricular response. Two years later, because of an episode of heart failure, he underwent echocardiography, which was consistent with restrictive cardiomyopathy, and an abdominal fat biopsy with positive results, leading to the diagnosis of AL amyloidosis. Over the next 2 years, the patient presented with several episodes of orthostatic syncope and hospitalizations for heart counterpulsation until emergency CTx could be performed. Following a postoperative period initially complicated by renal failure, he was discharged in excellent clinical and analytical condition. At 7 months post-transplantation, autologous bone marrow transplantation (BMT) was performed, with a temporary reduction in immunosuppressive drugs to favor stem cell mobilization, which were infused 1 month later, following preparation with intravenous melphalan and prednisone. At discharge, the patient was asymptomatic and immunosuppressant concentrations were adequate, but 2 weeks later he died suddenly in his home. The autopsy showed severe cellular rejection in the heart graft.
DISCUSSION

In primary or AL amyloidosis, the amyloid substance is formed by light chains of immunoglobulins produced by plasma cell dyscrasia. Although the infiltration usually affects several organs, the heart is involved in more than 50% of cases and this implies a devastating prognosis, with a median survival of 6 months following the diagnosis. Support treatment for the associated heart failure is based on diuretics. Angiotensin-converting enzyme inhibitors and beta-blockers are poorly tolerated in patients with symptomatic hypotension, and calcium channel blockers are not advisable because of their tendency to bind with the anomalous protein.1 Treatment directed against the plasma cell clone can halt protein deposition and even revert the deposits already formed, in addition to improving function of the affected organs. The most commonly used drugs for this condition are melphalan and prednisone, although...
diflunisal achieve stabilization of transthyretin and prevent amyloid formation in vitro. Nonetheless, in clinical practice, there is no specific treatment for this type of amyloidosis, apart from CTx in cases of advanced heart failure and LTx to eliminate the amyloid-producing organ (patient 2). Identification of carriers of the anomalous gene in family members of patients with ATTR can enable LTx to be performed in the early, initial phase of heart or nervous system involvement.

There are other types of amyloidosis, such as secondary or AA amyloidosis, which appears in situations of chronic inflammation and usually does not affect the heart, and senile amyloidosis, which is rare in patients younger than 60 and is not generally treated with CTx.

In conclusion, the development of techniques to identify the type of CA and monitor the response to treatment, the development of drugs able to decrease amyloid production and favor regression of existing deposits, and above all, the formation of multidisciplinary teams specialized in the management of this type of disease, which includes multiple organ transplantation, open a door to hope for the future in patients with AC.

REFERENCES