CASE REPORT

Cardiac Sarcoidosis: Recurrence in a Heart Transplant Recipient

CÉSAR A. BELZITI[MTSAC, 1], SEBASTIÁN MALDONADO[1], NORBERTO VULCANO[MTSAC, 1], DIEGO PÉREZ DE ARENAZA[1], RICARDO MARENCHINO[2], ALBERTO DOMENECH[MTSAC, 2], HERNÁN GARCÍA RIVELLO[3]

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Address for reprints:
Dr. César A. Belziti
Hospital Italiano de Buenos Aires
Servicio de Cardiología
Gascón 450
(C1181ACH) Buenos Aires,
Argentina
e-mail: cesar.belziti@
hospitalitaliano.org.ar

SUMMARY

Cardiac sarcoidosis is a multisystemic granulomatous disease of unknown etiology. Isolated cardiac involvement is rare and the prognosis correlates with the extension of heart compromise. Immunosuppressive treatment and heart transplantation have demonstrated to improve survival; however, the presence of recurrences in heart transplant recipients has been reported. We describe a recurrence of cardiac sarcoidosis in a patient with advanced dilated cardiomyopathy who underwent heart transplantation. The diagnosis of sarcoidosis was made by histopathological study of the explanted heart. The patient had a favorable clinical course despite the recurrence of sarcoidosis in the transplanted heart.

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Key words > Dilated Cardiomyopathy - Sarcoidosis - Magnetic Resonance Imaging - Heart Transplantation

Abbreviations >

AV	Atrioventricular	**ECG**	ECG Electrocardiogram
EMB	Endomyocardial biospsy	**DCM**	Dilated cardiomyopathy
FC	Functional class	**CS**	Cardiac sarcoidosis

BACKGROUND

The absence of systemic involvement in cardiac sarcoidosis (CS) is rare. This condition may be asymptomatic or may present with ventricular arrhythmias, atrioventricular blocks, heart failure or sudden death. The diagnosis of the disease is based on the criteria established in 1993 by the Japanese Ministry of Health and Welfare. (1) The sensitivity of endomyocardial biopsy (EMB) is very low despite being the gold standard method for the diagnosis of CS. With the advent of diagnostic imaging techniques, new strategies are being developed to complement the diagnosis of the disease. Immunosuppressive treatment has increased survival; however, some patients evolve with end-stage heart failure, and heart transplantation is the only possible treatment for these patients. The low prevalence of the disease makes it difficult to develop randomized and prospective trials; for this reason, current evidence comes from series. We describe the case of a patient with CS who underwent heart transplantation due to end-stage heart failure and presented recurrence of the disease in the graft.

CASE REPORT

A permanent dual-chamber pacemaker was implanted to a 46-year old man without history of cardiovascular risk factors in 2002 due to complete AV block. He complained of effort dyspnea at the end of 2003. A diagnosis of dilated cardiomyopathy with severe left ventricular dysfunction was made. The patient did not have associated valvular disease. Coronary angiography showed normal coronary arteries, and serologic studies for Chagas-Mazza disease and virus infections were negative. A diagnosis of idiopathic dilated cardiomyopathy was made and full treatment was initiated. The patient was hospitalized several times due to heart failure with requirement of inotropic drugs. In November 2008, the patient received cardiac resynchronization therapy with an implantable cardioverter defibrillator due to presyncope, FC III-IV dyspnea and episodes of non-sustained ventricular tachycardia. One month later he was hospitalized due to severe heart failure with low cardiac output syndrome unresponsive to inotropic drugs. For this reason, he was referred to our institution for hemodynamic support and evaluation of heart transplantation. The echocardiogram showed biventricular dilatation, severe left ventricular dysfunction and mitral regurgitation secondary to mitral annular dilatation. He

Hospital Italiano de Buenos Aires, Argentina
[MTSAC] Full Member of the Argentine Society of Cardiology
[1] Department of Cardiology
[2]Department of Cardiovascular Surgery
[3]Department of Anatomical Pathology

required mechanical circulatory assistance with intraaortic balloon pump and was placed on the emergency transplant list. He underwent orthotopic heart transplantation on January 5, 2009, with favorable postoperative outcomes. The histopathologic study of the explanted heart showed the typical findings of CS: signs of myocarditis with non-necrotizing granulomas constituted by giant multinucleated cells among areas of fibrosis. The infectious etiology was ruled out using complementary techniques for fungi and acid-fast bacilli (Figure 1). Immunosuppressive therapy with meprednisone, mycophenolate sodium and cyclosporine was initiated. The first endomyocardial biopsies were negative for rejection and there were no abnormal granulomatous infiltrates. A control biopsy performed at the third month showed focal infiltration with granulomas similar to those previously described; a diagnosis of CS in the heart graft was made.

Computed tomography of the chest and abdomen did not show lung or lymphatic involvement. By that time, immunosuppressive therapy consisted of meprednisone, 10 mg/day, mycophenolate sodium, 70 mg bid and cyclosporine, 90 mg bid with adequate blood levels of cyclosporine. Echocardiography revealed the presence of normal cardiac diameters and ventricular function; the latter was also normal at cardiac magnetic resonance imaging; yet, late gadolinium enhancement with a subepicardial and intramyocardial patchy pattern in the anterolateral and inferolateral segments was observed, indicating the presence of myocardial fibrosis or inflammation (Figure 2). Immunosuppressive treatment was optimized and higher doses were administered. Eleven months after transplantation, the patient is asymptomatic, without signs of heart failure, with preserved ventricular function, good functional capacity and normal subsequent EMBs.

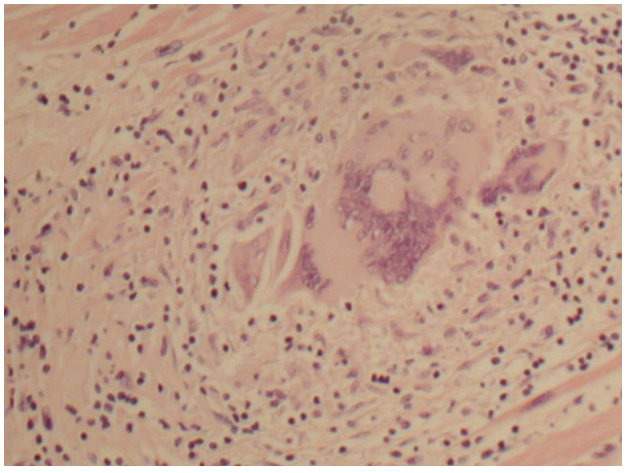

Fig. 1. Histological image of EMB. Inflammatory cells forming non-necrotizing granulomas and multinucleated giant cells can be seen (arrows).

DISCUSSION

Cardiac sarcoidosis is a chronic inflammatory cardiomyopathy with a low prevalence but highly lethal, that affects patients with a previous diagnosis of pulmonary or systemic sarcoidosis. Isolated CS is rare. Hagemann et al. reported that the prevalence of cardiac manifestations in patients with systemic sarcoidosis was 5%. However, Thomsen et al. demonstrated that heart involvement was present in 50% of autopsy cases with systemic sarcoidosis. (2, 3) The diagnosis of CS is a challenge, as symptoms may develop before, during or after the presentation of systemic symptoms. (3) CS should be suspected in young patients with congestive heart failure associated with advanced AV block, ventricular arrhythmias, abnormal ventricular thickening, wall motion abnormalities or rest perfusion defects in the anteroseptal and apical segments that are reversible with exercise (reverse distribution phenomenon). In addition, pericardium may also be involved. Infiltration of papillary muscles and great vessels produce valvular dysfunction and arteritis, respectively. (3) Diagnostic strategies include ECG, echocardiography, myocardial imaging with 201Thallium and EMB. Despite its low sensitivity, EMB should be performed in all patients with suspicion of CS, as it is the gold standard diagnostic method and is useful to rule out other conditions with similar clinical and histopathological manifestations, as giant cell myocarditis, which has worse prognosis. (4) However, the diagnosis of CS can be confirmed with a positive EMB and at least another of the

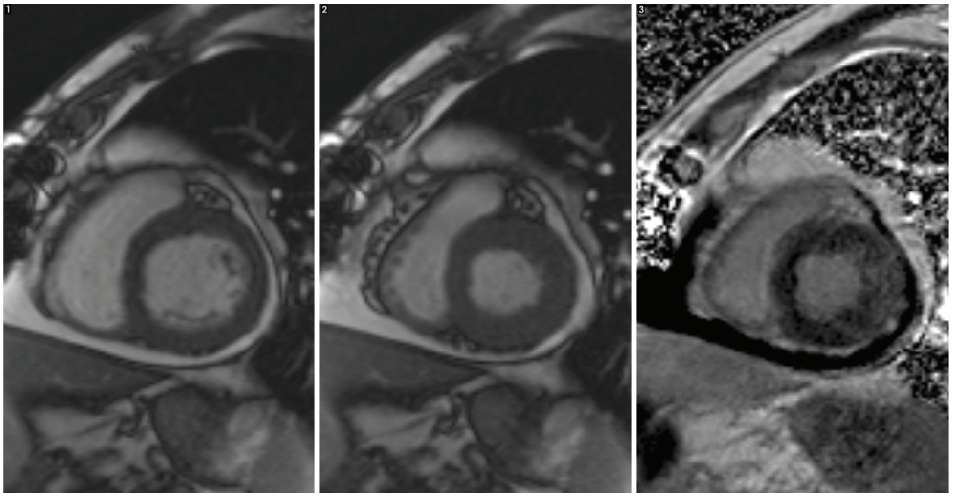

Fig. 1. Cardiac magnetic resonance images. Baseline images with normal regional wall mation (A: end-diastole, B: end-systole). Late gadolinium enhancement image (C) showing a patchy intramyocardial pattern in basal inferolateral and anterolateral segments (arrows).

previously mentioned studies with typical finding of CS. (5) Delayed contrast-enhanced cardiac magnetic resonance imaging is useful to detect fibrosis, necrosis, inflammation or edema. (6, 7) In CS, delayed enhacement has a subepicardial and intramyocardial patchy pattern in the basal segments that does not correspond to a coronary territory, as opposed to infarction due to vascular oclusion. (8)

Heart transplantation is the only alternative for patients with CS and end-stage heart failure. In a retrospective analysis of heart transplantations due to CS in the United Kingdom, Saidi et al. demonstrated survival rates at 1 year and 40 months of 87% and 75%, respectively. (9) Cases of recurrence of sarcoidosis in the transplanted heart have been reported. However, current immunosuppressive therapy may control the disease with favorable long-term outcomes. For this reason, heart transplantation is still a valid therapeutic option for stage CS. (10)

CONCLUSIONS

CS is a rare chronic inflammatory cardiomyopathy which can evolve to end-stage heart failure with requirement of heart transplantation. Despite the recurrence described in the implanted heart, this treatment improves quality of life and life expectancy. Cardiac magnetic resonance imaging provides useful information for the evaluation of patients with suspicion of CS, as gadolinium enhancement may detect areas of inflammation and fibrosis.

RESUMEN

Sarcoidosis cardíaca: descripción de tres casos

La sarcoidosis cardíaca es una enfermedad granulomatosa multisistémica de causa desconocida. El compromiso aislado del corazón es poco frecuente y el pronóstico se correlaciona con el grado de afectación de este órgano. El tratamiento inmunosupresor y el trasplante cardíaco han demostrado que prolongan la sobrevida; no obstante, existen comunicaciones de recidiva de la enfermedad en el órgano implantado. En esta presentación se describe un caso de recidiva de sarcoidosis cardíaca en un paciente con miocardiopatía dilatada con insuficiencia cardíaca avanzada, sometido a un trasplante cardíaco y en quien el diagnóstico de sarcoidosis cardíaca se estableció por el estudio anatomopatológico del corazón explantado. La evolución clínica fue favorable a pesar de la recidiva de la sarcoidosis en el órgano implantado.

Palabras clave > Sarcoidosis - Granuloma - Arritmia cardíaca - Insuficiencia cardíaca

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