

Case Report

An idiopathic myocardialopathy case-control patient submitted to autologous stem cells implant – case report

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The heart failure (HF) is a syndrome in which the heart becomes incapable of supplying enough oxygen to the tissues. The case of a 42-year old male patient with idiopathic dilated myocardialopathy (ECG – sinus rhythm with typical left bundle branch block and duration of QRS=160msec), progressive worsening of clinical history, going through a period of 24 months from functional class II to IV, in spite of the therapeutic optimization until becoming refract. One month later, Gated showed Left Volume Ejection Fraction (LVEF) of 18%, with moderate asynchronism between right / left ventricle and left interventricle. The artificial cardiac resynchronization implant on was realized and followed for an autologous bone marrow stem-cells (BMSCs) via intracoronary. While the hemodynamicist was getting ready for the implant of the same cells in the right coronary artery, the patient developed ventricle fibrillation rhythm with the need of exam suspension for cardiorespiratory resuscitation. Gated showed a little improvement of LVEF (22%), however, an interesting fact was observed: the walls that received the cells had a significant response with contraction improvement which did not reflect in the overall outcome because of the worsening of the walls irrigated by the right coronary artery that did not receive the cells.

Keywords: Heart Failure, Myocardialopathy, Left Volume Ejection Fraction, Gated, Bone Marrow Stem-Cells.

INTRODUCTION

Heart failure (HF) is generally defined as inability of the heart to maintain cardiac output sufficient to meet the body's needs; it most often results from myocardial failure affecting the right or left ventricle (Merck, 2010). Dilated cardiomyopathy is a disease without effective therapeutic options in addition to cardiac transplantation. Unfortunately, organ rates are low and most of the patients on transplant waiting list died before receiving a new heart. Therefore, a therapy capable of improving cardiac function and more accessible to the population is of great interest (Soares and Santos, 2010).

Nowadays, in addition to the hemodynamics and neuro-hormonal concepts, the inflammatory context

identified in this complex syndrome represented by release of interleukins and tumor necrosis factor (TNF), characterize hypercatabolism state and a consequent worse prognosis. The HF can also be more clearly defined in acute manner, uncompensated chronic and refract (Cleland and Clark, 1999; Swedberg et al., 2005; Jessup and Bronzena, 2007).

Studies in ischemic heart disease demonstrated that stem cells obtained from various sources, including bone marrow, can contribute indirectly to cardiac regeneration (Leri et al., 2006), and indicated the potential use of stem cell therapy in other cardiomyopathies. Stem cell therapy has emerged as a potential therapeutic option for cell death-related heart diseases and several positive effects were assigned to cell therapy in cardiomyopathy (Dib et al., 2005; Barbash and Leor, 2006) like as: improvement of left volume ejection fraction (LVEF), decreasing end-diastolic and systolic volumes, myogenesis and

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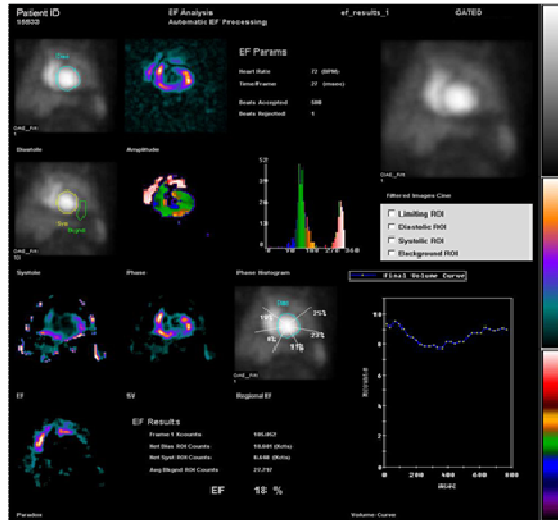


Figure 1. Gated before the artificial cardiac synchronizer and bone marrow stem cells implants

The image showed Left Volume Ejection Fraction (LVEF) of 18%, with moderate assynchronism between right / left ventricle and left interventricle. (Millennium MPR, GE, series # 40114)

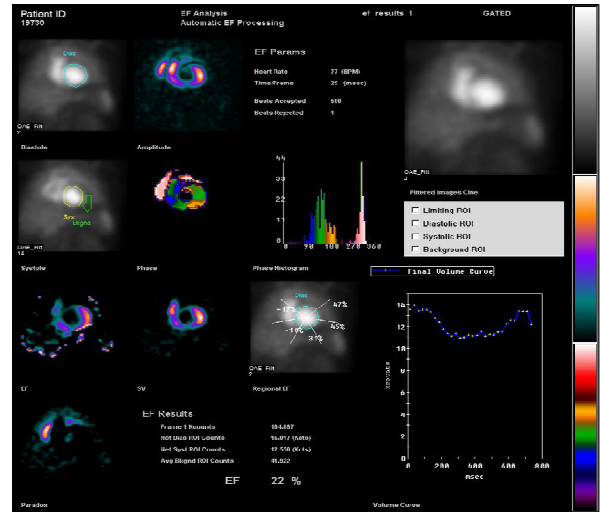


Figure 2. Gated post-procedures

The image showed a slight Left Volume Ejection Fraction (LVEF) of 22%. The left ventricle walls, that received the bone marrow stem cells implant, had a significant response, with good contraction improvement. (Millennium MPR, GE, series # 40114)

angiogenesis, after treatment (Dib et al., 2005; Barbash and Leor, 2006; van Ramshorst et al., 2009a, b).

CASE REPORT

A 42-year old male patient with idiopathic dilated cardiomyopathy (ECG – sinus rhythm with typical left branch block and duration of QRS=160msec), progressive worsening of clinical history, going through a period of 24 months from New York Health Association (NYHA) functional class II to IV, in spite of the therapeutic optimization until becoming refract. One month later, Gated (Millennium MPR, GE, series # 40114) showed Left Volume Ejection Fraction (LVEF) of 18%, with moderate assynchronism between right / left ventricle and left interventricle (Figure 1).

The patient followed all ethical guidelines of National Research Ethics Committee (CONEP Number: 15342), then the cardiac synchronizer implant (an arm of the Clinical Trial “Stem Cells and Resynchronization Cardiac (RCT and SCT)”, # NCT00800657) was followed by autologous bone marrow stem-cells (BMSC) transplantation, via intracoronary. On the day of the injection procedure (after two months of cardiac synchronizer implant), 125 mL of bone marrow was harvested from each patient. The bone marrow was aspirated from the iliac crest by an experienced hematologist under peridural anesthesia and placed in a heparinized Hanks balanced salt solution. The mononuclear cells were isolated using Ficoll-Paque (GE Health care Biosciences AB Upsala, catalog # 17544203)

density gradient centrifugation (1500 rpm, 30 minutes, 18°C), according to good manufacturing practice regulations, washed in phosphate buffered saline with 0.5% human serum albumin, and resuspended in phosphate buffered saline with 5% human serum albumin. The final suspension of bone marrow mononuclear cells contained 3.0×10^8 cells (5.0×10^6 CD 34+ and 2.5×10^6 CD 133+) was injected in the affected area. Before every injection, the catheter was positioned perpendicular to the endocardium with excellent loop stability and the extension of the needle had to induce a premature ventricle contraction. During the stem cell implant, the hemodynamicist had just injected BMSC in the left coronary artery, using its descendent anterior dominant branch, when patient developed ventricle fibrillation rhythm and the procedure was interrupted for cardiorespiratory resuscitation. Due to this complication, the BMSC implant in the right coronary artery was not performed. The patient was in hospital for five days and went home in good health, without sequelae.

He was accompanied by an outpatient basis, for a year and returned to NYHA functional class II. The post-procedure exams were repeated and the Gated showed a slight LVEF improvement (from 18% to 22%). However, another interesting fact could be observed: the walls which received the BMSC had a significant response, with good contraction improvement, though this fact was not reflected in the overall result, since the walls irrigated by the right coronary artery did not received the cells and worsened (Figure 2). By this situation, we recommend new BMSC implant, emphasizing areas irrigated by the right coronary artery.

DISCUSSION

In the last few years, a great interest in the therapeutic use of stem-cells in the cardiac tissue repair after the myocardial infarct has reflected in the increase of papers on basic research, pro-clinic and clinical, published in international publications (Dib et al., 2005; Barbash and Leor, 2006; van Ramshorst et al., 2009a, b).

However, the researchers still don't know how to explain the mechanisms of the cells act, the benefit represented by each cell type injected, as well as the number of cells that should be used and the therapeutic window of its application (Assmus et al., 2006).

As a pioneer, the transplant of skeleton muscle satellite cells was performed to the heart of an elderly refractory heart failure patient. However although favorable results in a short-term analysis, patients treated with satellite cells present, in the long term, adverse effects such as arrhythmias due to the lack of injected cells integration with the healthy tissue of the graft recipient (Menasché et al., 2001).

The transcatheter injection of mononuclear cells in chronic infarct tissue of the myocardium showed a safe and efficacious procedure, speeding up the process of the cardiac muscle regeneration and recovering the heart mechanical properties. Apparently, the main role of these cells is to promote the revascularization of the tissue and the direct or indirect recovery of the cardiomyocytes (paracrine effect) (Dohmann et al., 2005).

Strauer and coworker (2002), during the coronary angioplasty of 10 patients with acute myocardium infarct BMSC transplanted, injected these cells into the artery that irrigates the region through a balloon catheter. In the first three follow-up months, there was a decrease of the infarct area (left ventriculography), in addition to the increase of contractility of the affected wall.

Recent studies show that autologous BMSC infused via intracoronary or intramyocardial represent a possible strategy to the ventricle dysfunction reversion, especially post-infarct, stimulating the neovascularization in the infarct area with consequent perfusion improvement in the chronic ischemic area and increase of the systolic function of the left ventricle (Dawn and Bolli, 2007).

In a reported case was observed after the infusion BMSC by intracoronary technique, a significant number of such cells is attracted and retained to specific areas, showing that the distribution of mononuclear cells, labeled with ^{99m}Tc -HMPAO, was intense uptake by the heart muscle and the remainder mainly in the liver and spleen (Jacob et al., 2007). During a four years follow-up study, myoblasts were successfully transplanted in ischemic cardiomyopathy patients and echocardiography measured an average change in LVEF from 28% to 35% at 1 year and of 36% at 2 years (Dib et al., 2005) The LVEF improvement was also observed in severe postinfarction heart failure patients submitted to BMSC infusion (van Ramshorst et al., 2009a). Data of the

present study corroborate the literature, because the analysis of the left ventricle ejection fraction indicates a slight improvement in cardiac function (2%) and good contraction improvement, in the left walls, where the BMSC was transplanted.

The stem-cells represent one of the great promises of the future medicine with treatment proposals of different diseases considered as no therapeutic options. Their main role would be the regeneration of impaired function organs by processes of different etiologies: inflammatory, traumatic and degenerative. Based on recent studies this potential will eventually provide treatment to neurological, cardiovascular and skeletal muscle diseases (Assmus et al., 2006).

An interesting revision of the main studies that evaluated the response to the cardiac resynchronization stresses that the use of the presence alone of electric dissynchrony as a selection criteria, a method used and updated today for the procedure reference, has promoted a clinically significant improvement for the HF sufferers (Cleland et al., 2001). It also shows that in small studies of casuistic case series in isolated centers, the use of presence criteria of mechanical dissynchrony for cardiac resynchronization reference has promoted more consistent results when we provide the association with cell therapy (Cleland et al., 2001; Hawkins et al., 2006).

CONCLUSION

We believe that BMSC is a safe procedure and possible to be applied in patients with dilated cardiomyopathy refractory to conventional therapeutics, because we noted a positive response in the patient, with true functional improvement of the wall that received the cells in comparison to the one that did not receive it.

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