

# The Evolution of Intracardiac Hemodynamics Post Autologous Stem Cell Transplant in a Case of Multiple Myeloma Associated with Severe Tricuspid and Mitral Valve Insufficiency

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## ARTICLE HISTORY

Received: October 23, 2017  
Accepted: November 23, 2017

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## ABSTRACT

Stem cells are undifferentiated cells that can divide and become differentiated. Hematopoietic stem cells cannot transform into new stem cells such as cardiomyocytes or new heart valves, but they act through paracrine effects, by secreting cytokines and growth factors that lead to an increase in contractility and overall improved function. In this case report, we present how autologous stem cell transplantation can bring two major benefits: the first refers to hematological malignancy and the second is about the improvement of the heart condition. We present the case of a 60-year-old patient diagnosed with multiple myeloma suffering from a bi-valve severe condition in which autologous stem cell transplantation led to the remission of the patient's malignant disease and also improved the heart function.

**Keywords:** multiple myeloma, autologous stem cell transplantation, valve insufficiency

## INTRODUCTION

Multiple myeloma was first described by Solly in 1844 and is one of the most common malignant diseases that usually appear at old age (>65 years).<sup>1</sup> In recent years, the incidence started to grow in younger patients. It represents approximately 10% of the hematological malignancies and 1% of all malignancies.<sup>2</sup> It is characterized by the proliferation of malignant plasma cells and overproduction of a monoclonal paraprotein (M protein). Until the present day, the disease is considered to be treatable, but incurable.<sup>3</sup> Since 1975, the Durie-Salmon staging system has been used to stratify patients with multi-

ple myeloma. Serum beta 2-microglobulin, serum albumin, thrombocyte count, serum creatinine, and age have emerged as powerful predictors of survival and have led to the creation of this International Staging System (ISS) that comprises three stages. The first stage is defined by a serum beta 2-microglobulin value of under 3.5 mg/L and albumin levels of 3.5 g/dL, in which the mean survival rate is up to 62 months; the second stage is intermediary between the first and last; and the third stage includes a level of beta 2-microglobulin of over 5.5 mg/L, leading to a median survival of 29 months.<sup>4,5</sup> The ISS staging method was later confirmed on subjects  $\leq 65$  years of age, in subjects with standard therapy, or autotransplantation in comparison with the Salmon/Durie staging method.<sup>6</sup> The treatment of multiple myeloma is very vast and includes chemotherapy, immune therapy, radiation therapy, surgery, or a combination of these, as well as the novel use of stem cell transplantation.<sup>7-9</sup>

Tricuspid insufficiency, also known as tricuspid regurgitation or tricuspid valve incompetence, is a valve disease described by the incomplete closure of the cusps during the cardiac systole, causing the blood to leak backwards from the right ventricle to the right atrium. It is considered to be functional (secondary) in the majority of the cases or organic (primary) in the rest. Mitral valve insufficiency or mitral valve regurgitation is a condition in which the heart mitral valve does not close tightly during the systole which causes the blood to leak upwards from the left ventricle to the left atrium.<sup>10,11</sup>

## CASE REPORT

We present the case of a 60-year-old patient diagnosed with stage I/B  $\lambda$  light chain multiple myeloma, also suffering of secondary severe anemia, moderate thrombocytopenia, stage II chronic kidney disease, B-virus chronic hepatitis, and moderate/severe mitral valve insufficiency associated with severe tricuspid insufficiency, who benefited from autologous stem cell transplantation.

After the admittance, the patient presented symptoms related to congestive heart failure such as severe fatigue, dyspnea, orthopnea, jugular pulsation, hepatomegaly of stasis, and edema. The clinical examination of the cardiovascular system revealed holosystolic murmur at the apex, radiating to the axilla. The blood analyses revealed anemia, thrombocytopenia, and high levels of creatinine and urea. The ultrasound examination of the abdomen revealed stasis of the liver.

Because of the cardiotoxicity of the conditioning regimen (HD-melphalan) and because the patient was already

treated with cardiotoxic drugs (cyclophosphamide), the patient was overseen by a cardiologist before administering the conditioning regimen.

The transthoracic echocardiographic examination conducted five days before the stem cell transplantation revealed the following: right ventricle diameter 36 mm, left ventricle 56/38 mm, interventricular septum 8/11 mm, posterior wall 10/13 mm, aortic annulus 19 mm, ascendant aorta 29 mm, ejection fraction 50%, left atrium area 38 cm<sup>2</sup>, left ventricle/left atrium gradient 45 mmHg, pulmonary artery pressure 65 mmHg; mitral valve – moderate/severe regurgitation; tricuspid valve – severe regurgitation; mitral valve prolapse with moderate to severe regurgitation; aortic valve – supple, mobile, opened in M mode cusps, aortic valve opening 22 mm; pericardium with posterior echo-free space of 6 mm, with increased echogenicity; inferior vena cava 31 mm, without inspiratory collapse present and dilated suprahepatic veins. The final diagnosis of the transthoracic echocardiography included the presence of moderate to severe mitral regurgitation, severe tricuspid regurgitation, and severe pulmonary hypertension.

The standard conditioning regimen consists of HD-melphalan with a mean of 200 mg/m<sup>2</sup>, but because of the cardiac condition of the patient the dose was lowered to 140 mg/m<sup>2</sup>, consisting in a total dose of 274 mg melphalan. Two days after chemotherapy, the patient benefited from the reinfusion of the stem cells through a central venous catheter. The total quantity of the harvested cells was  $5.54 \times 10^6$ /kg body weight, and the patient benefited of  $3.17 \times 10^6$ /kg body weight, which is more than enough for a successful procedure. As a complication of the stem cell transplantation, the patient presented nausea, vomiting, and diarrhea, which led to electrolyte disorders, including hypokalemia and hypocalcemia, which needed rebalancing.

Twelve days after the stem cell transplantation, the patient was overseen again by the same cardiologist, and the transthoracic echocardiographic examination was repeated, with the following findings: left atrium area 32 cm<sup>2</sup>, ejection fraction 60%, moderate mitral regurgitation, regurgitation area 6 cm<sup>2</sup>, mild tricuspid regurgitation, pulmonary artery pressure 55 mmHg, without vegetations. This time, the echocardiographic examination concluded in a diagnosis of moderate mitral regurgitation, mild tricuspid regurgitation and mild pulmonary hypertension, and minimum pericardial liquid, thus showing significant improvement since the last echocardiography that was performed before stem cell transplantation.

The patient was released 7 days later in a good general state, with laboratory blood tests within normal range and with an improved heart condition. The patient agreed to the publication of his data and the institution where the patient had been admitted, approved the publication of the case.

## CONCLUSION

Due to the pluripotent properties of stem cells, in the case presented in this article it is shown that not only the hematological malignancy represented by the multiple myeloma was efficiently treated but the heart condition was also obviously and objectively improved.

## CONFLICT OF INTEREST

Nothing to declare.

## REFERENCES

1. Kyle RA, Rajkumar SV. Multiple myeloma. *Blood*. 2008;111:2962-2972.
2. Becker N. Epidemiology of multiple myeloma. *Recent Results Cancer Res*. 2011;183:25-35.
3. Rajkumar SV. Multiple Myeloma. *Curr Probl Cancer*. 2009;33:7-64.
4. Durie BG, Salmon SE. A clinical staging system for multiple myeloma. Correlation of measured myeloma cell mass with presenting clinical features, response to treatment, and survival. *Cancer*. 1975;36:842-854.
5. Hari PN, Zhang M-J, Roy V, et al. [Is the international staging system superior to the Durie Salmon staging system? A comparison in multiple myeloma patients undergoing autologous transplant.](#) *Leukemia*. 2009;23:1528-1534.
6. Greipp PR, San Miguel J, Durie BG, et al. [International staging system for multiple myeloma.](#) *J Clin Oncol*. 2005;23:3412-3420.
7. San Miguel JF, Bladé Creixenti J, García-Sanz R. Treatment of multiple myeloma. *Haematologica*. 1999;84:36-58.
8. Fermand JP, Ravaud P, Chevret S, et al. High-dose therapy and autologous peripheral blood stem cell transplantation in multiple myeloma: up-front or rescue treatment? Results of a multicenter sequential randomized clinical trial. *Blood*. 1998;92:3131-3136.
9. Kyle RA, Rajkumar SV. Treatment of Multiple Myeloma: A Comprehensive Review. *Clinical lymphoma & myeloma*. 2009;9:278-288.
10. Rogers JH, Bolling SF. The Tricuspid Valve. *Circulation*. 2009;119: 2718.
11. Vahanian A, Alfieri O, Andreotti F, et al. Guidelines on the management of valvular heart disease. *Eur Heart J*. 2012;33:2451-2496.