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Brief Communication

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Stem cell therapy for congestive heart failure

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Introduction

Heart failure is a major cardiovascular health problem. Coronary artery disease is the leading cause of congestive heart failure (CHF) [1]. Cardiac transplantation remains the most effective long-term treatment option, however is limited primarily by donor availability, rejection and infections. Mechanical circulatory support has its own indications and limitations [2]. Therefore, there is a need to develop more effective therapeutic strategies.

Recently, regenerative medicine has received considerable scientific attention in the cardiovascular arena. We report here our experience demonstrating the beneficial effects of cardiac stem cell therapy on left ventricular functions in a patient with Hodgkin's lymphoma (HL) who developed CHF due to ischemic heart disease during the course of lymphoma treatment.

Case report

A 58-year-old male with relapsed HL was referred to our bone marrow transplantation unit in October 2009. He was given 8 courses of combination chemotherapy with doxorubicin, bleomycin, vincristine, and dacarbazine (ABVD) between June 2008 and February 2009 and achieved complete remission. However, his disease relapsed 3 months after completing the last cycle of ABVD and he was decided to be treated with DHAP (cisplatin, cytarabine, dexamethasone) followed autologous stem cell transplantation (SCT). After the completion of first course of DHAP regimen, he developed acute myocardial infarction (AMI) and coronary artery bypass grafting (CABG) was performed. After his cardiac function stabilized, 3 additional courses of DHAP were given and he was referred to our centre for consideration of autologous SCT. Computed tomography scans obtained after chemotherapy confirmed

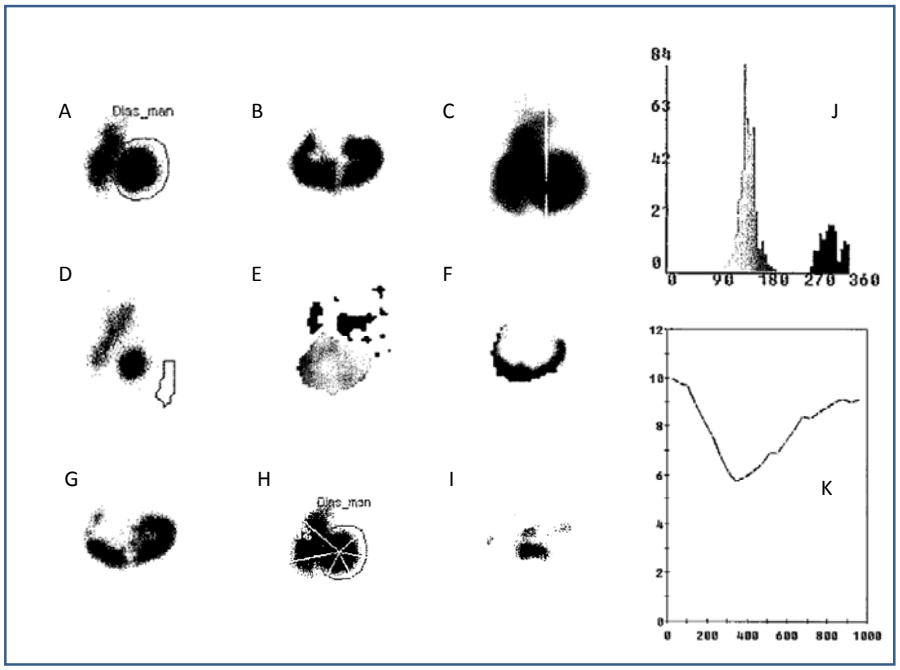

Figure 1. MUGA scan obtained during the last evaluation before stem cell transplantation

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complete remission. Stem cells were collected from peripheral blood after mobilization with 10 µg/kg/day granulocyte colony-stimulating factor (G-CSF) subcutaneously. Collection was started on the fifth day of G-CSF and performed for 3 consecutive days. Flow cytometric analysis of CD 34 was used to identify hematopoietic stem cells. During the last evaluation before stem cell transplantation, conventional echocardiogram (ECHO) revealed left ventricular systolic dysfunction with an ejection fraction of ALEF: 44%, MODEF: 45%, MUGA scan showed a decreased left ventricular ejection fraction (LVEF: 43%) (Figure 1).

In view of these findings, the patient was found ineligible for SCT and he was offered to give his peripheral blood stem cells for the treatment of heart failure. After receiving the patient's signed informed consent form, a total number of $3.49x10^6$/kg CD 34^+ cells were infused via antecubital vein. Echocardiographic studies performed 2 months after stem cell therapy revealed a similar ejection fraction rate while a significant improvement in left ventricular ejection fraction (ALEF: 55%, MODEF: 57%) was noticed in ECHO performed 7 months after stem cell therapy (Figure 2).

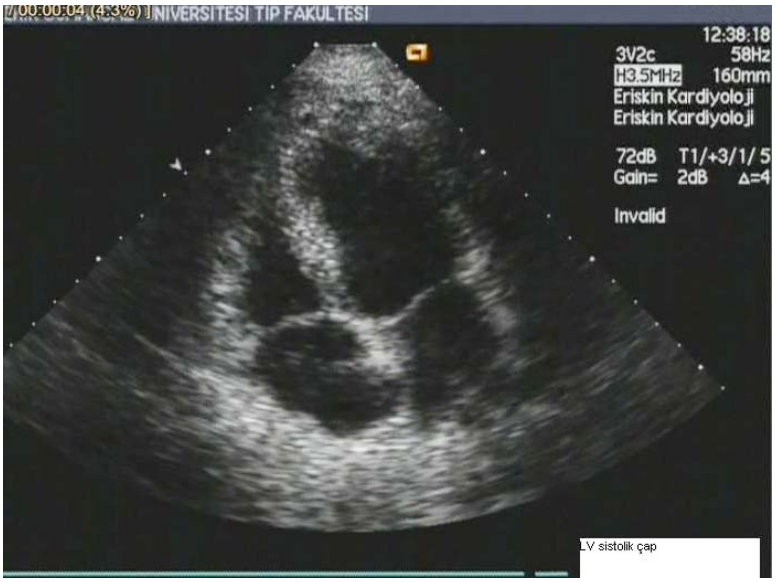

Figure 2: ECHO performed 7 months after stem cell therapy

EF values at various time periods are shown on Table 1. Myocardial perfusion scintigraphy was also performed and showed infarction containing viable tissue in inferior wall (Figure 3). Myocardial positron emission tomography revealed that glucose metabolism was conserved in inferior wall.

HL was in complete remission in the 2 months follow up after SCT but SCT for HL was not contemplated because renal failure due to chemotherapy developed later.

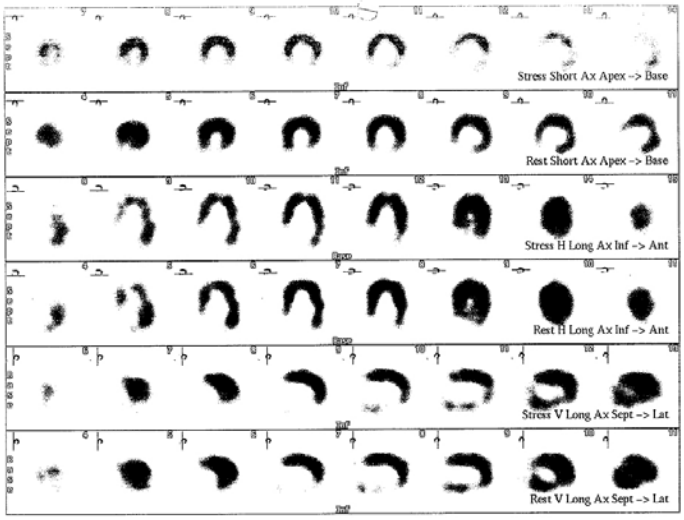

Figure 3. Myocardial perfusion scintigraphy after stem cell therapy

Discussion

Here, we reported a patient with HL who was ineligible for SCT because of low LVEF due to AMI. LVEF was low despite CABG. Collected stem cells were used as a stem cell therapy for heart failure since he was ineligible for SCT directed to treat HL. Although intravenous infusion of stem/progenitor cells are not favoured any more and intracoronary infusion or intramyocardial injections are preferred in latest reports [3] our data supports this route can still be effective.

The objective of stem cell therapy in CHF due to ischemic heart disease is to repopulate post-infarction scar tissue with contractile cells that can engraft in sufficient numbers to differentiate to the cardiac myocytes and restore functionality in these akinetic areas. Hematopoietic stem cells consist can differentiate to skeletal and myocardial cells when cultured under appropriate conditions [4].

Strauer et al [5] reported that intracoronary bone marrow stem cell therapy improves ventricular performance, quality of life and survival in patients with chronic heart failure. Hamano et al [6] showed in 5 patients that autologous bone marrow cells can be injected safely during a by-pass operation into areas of ischemic myocardium. Brehm et al [7] have treated 23 patients with acute cardiac infarction using autologous mononuclear bone marrow cells. Ozbaran et al [8] transplanted peripheral blood stem cells into areas of injury with open-heart surgery in six patients with ischemic cardiomyopathy.

Table 1: EF values at various time periods

	Ejection Fraction	
	ECHO	MUGA
Before SCT	44%	43%
2 months after SCT	46%	
7 months after SCT	55%	

There are also meta-analysis on ongoing clinical trials performed. Abdel-Latif et al [9] described a statistically significant improvement in ejection fraction, reduction in infarct size and left ventricular end-systolic volume in 18 patients treated with either unseparated bone marrow cells, bone marrow mesenchymal and mobilized peripheral blood cells. Martin-Rendon et al [10] focused on 13 randomized studies encompassing 811 participants on bone marrow therapy for post acute infarction. Improvement in LVEF, decrease in left ventricular and systolic and end diastolic volumes and infarct size were observed.

The reason for choice of intravenous route was being the standard way of giving hematopoietic stem cells by hematologists. We tried to decide the availibility of this route for indications other than hematological diseases. Although trapping of stem cells in the pulmonary vascular bed is a drawback of intravenous route and the question of whether the patient would have been more benefited by intracoronary or intramyocardial route remains unanswered, we think intravenous route may still have some role according to our own experience from this patient.

Conclusion

Studies in the era of cardiac stem cell therapy are heterogenous. It is not yet possible to comment on the most appropriate stem cell type and route of administration. When we assess the results from literature and the improvement in our own patient we think stem cell therapy can be an option for bridging to heart transplantation or an adjuvant therapy for CHF.

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