

EDITORIAL

Modern Hematology — a Complex Interdisciplinary Tool

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Hematological disorders are involved in a large number of systemic diseases in which complex interdisciplinary approaches are required to ensure the most effective treatment strategy. Stem cell therapy has emerged as a promising therapeutic tool, not only in patients with hematological disorders, but also in patients with acute myocardial infarction, severe heart failure, critical limb ischemia, neurological disorders, or for cartilage regeneration in various orthopedic applications.^{1,2} Modern bioengineering technologies made it possible to generate scaffolds impregnated with stem cells for various applications (such as patches for wound repair or for open heart surgery).^{3,4} It has also been demonstrated that in patients with heart failure or with coronary artery disease, correction of anemia can lead to a significant improvement of symptoms and outcomes.^{5,6}

Several hematological parameters carry also prognostic impact for other diseases. For instance, interventional cardiology studies demonstrated that neutrophil count, leucocyte count, or blood count-derived parameters such as red cell distribution width-platelet ratio (a new biomarker for inflammation) or neutrophil-lymphocyte ratio are significant predictors for the occurrence of no-reflow phenomenon after successful recanalization of an occluded coronary artery in the setting of an acute myocardial infarction.^{7–11}

Therefore, hematology can be considered as an important link between various diseases, serving also as a reflection of the severity of these pathologies. This special issue of JIM is focused on the most relevant topics in modern hematology.

Bzduch *et al.* performed a study on the importance of FLT3-ITD gene mutation in the survival of patients with acute myeloid leukemia (AML). The authors analyzed 210 patients with AML, from which 10 presented FLT3-ITD mutation, and the results showed an overall survival rate of 7% (n = 15), while patients with the specified mutation presented a 100% mortality rate (n = 10) within the first two months. Moreover, none of the subjects with FLT3-ITD mutation presented complete remission of the disease.¹²

Stem cell therapies have been used for the treatment of hematologic neoplastic diseases for over three decades, including Hodgkin and non-Hodgkin lymphomas.¹³ Pakucs *et al.* aimed to evaluate complications occurring after au-

tologous hematopoietic stem cell transplantation on 94 patients with malignant lymphomas. The analysis revealed that 18% of subjects presented confirmed infections, 42% presented electrolyte imbalances, and 36% had hypoalbuminemia.¹⁴ The results of this study underline the importance of a proper evaluation of complications that are related to stem cell therapies, in order to implement proper patient management.

Furthermore, Mild *et al.* performed a retrospective analysis on patients with failure of stem cell mobilization, in which the highest harvesting failure occurred in patients aged between 51 to 61 years, and all the analyzed subjects had been heavily pretreated with alkylating agents and purine analogs. Moreover, the study included patients with various types of hematological malignancies, and the results found that the highest mobilization failure occurred in non-Hodgkin lymphoma (42%, $n = 8$), Hodgkin lymphoma (37.5%, $n = 6$), and multiple myeloma (21%, $n = 4$).¹⁵ Being that autologous stem cell therapies can be a curative option for patients with various hematological cancers, further studies on the cause and factors associated with failure to harvest stem cells, as well as methods for improvement are essential.

Located at the border between hematology and cardiology, thrombosis and cardioembolic events in atrial fibrillation patients have been linked to increased systemic inflammation, hypercoagulable states, and enhanced atrial fibrosis.^{16,17} Oltean *et al.* are currently conducting a clinical observational study on atrial fibrillation patients, the FIBROS study, in which they will test the hypothesis that the degree of atrial fibrosis, in correlation with several hematological markers for inflammation, platelet aggregation, and clotting, could serve as a model for identifying the profile of patients at increased risk for cardioembolic events.¹⁸

Due to the versatile use of stem cells in various therapies, there has been an increasing interest in cellular applications, not only in hematological disorders, but also in non-healing ulcers, as well as in different types of peripheral artery disease.

This focus issue includes a case report on the effect of stem cell transplantation that led to improvement of both the hematological malignancy for which it was intended, but it also caused a significant improvement in the overall cardiac function. More specifically, Tudor *et al.* presented a patient with multiple myeloma, who went into the remission phase after stem cell transplantation, and presented an increase in the left ventricular ejection fraction from 50 to 60%, a smaller mitral regurgitation jet, and also a lower systolic pressure in the pulmonary artery.¹⁹ The success of

stem cell treatment on both the hematological condition as well as the associated cardiovascular condition is indicative of the pluripotent capacity of these novel treatments in complex patients with multiple comorbidities.

In an article published in this focus issue by Opincariu *et al.*, the authors sought to review the current articles on the use of stem cell treatments, not only on subjects with critical lower limb ischemia, but also on several types of peripheral artery disease, caused by either atherosclerosis or thromboangiitis obliterans, including upper limb ischemia, stroke patients, renal artery stenosis, and mesenteric ischemia.²⁰ The manuscript revealed the presence of extensive research on lower limb ischemia, which has shown promising results in restoring blood flow to no-option ischemic limbs, in which revascularization methods (surgical or interventional) either had failed, or were not suitable.²¹ At the same time, stem cells have been proven effective in improving motor deficits in ischemic stroke patients, but the main concern in these procedures is safety, the type of stem cell to be used, as well as the route of injection. Preclinical studies on swine and rat models are also cited by Opincariu *et al.* in stem cell therapeutic applications for renal artery stenosis and mesenteric ischemia, both showing promising results in the improvement of renal fibrosis and glomerular filtration rates, as well as increased survival and better recovery of the intestinal barrier after induced intestinal ischemia.^{22,23}

Another manuscript in this issue is concerning the use of cell therapies in non-healing ulcers, published by Mester *et al.* The authors present a clinical update on the use of various types of stem cells, harvested from the bone marrow, adipose tissue, umbilical cord, and placenta, that present paracrine effects, trigger angiogenesis, cell proliferation, and tissue regeneration, thus inducing ulcer healing and epithelization, while simultaneously decreasing the local fibrosis.²⁴ There is multiple evidence regarding the efficacy of stem cells in the improvement of various types of non-healing wounds caused by skin cancer, irradiation, diabetes, and ischemia, leading to the belief that stem cells could become a first line of treatment in chronic ulcers that present no tendency for regeneration.²⁵⁻²⁸

All three manuscripts present possible prospects in stem cell therapies in hematological diseases, complex cardiovascular disorders, peripheral artery disease, and non-healing wounds, describing the emerging use of allogeneic cells from matched HLA healthy donors, as well as the ethical and financial limitations of these methods. However, all authors mention the great therapeutic potential of stem cells in disorders in which other treatment methods have failed.

Novel therapies in various diseases that include stem cell transplantation require a proper collaboration between a multitude of specialties. Stem cell harvesting and mobilization for their use in cardiac and vascular disorders are performed with the help several specialists including the hematologist. Various cardiovascular diseases are influenced by hematological parameters, while hematological disorders and their treatment can have great impact on the cardiovascular balance, thus underlying once again the importance of a proper collaboration between specialties for both a proper patient management, as well as in preclinical and clinical research.

CONFLICT OF INTEREST

Nothing to declare.

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