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Hematopoietic stem cell transplantation (HSCT): An approach to autoimmunity

Carmen Alaez [a], Mariana Loyola [a], Andrea Murguía [a], Hilario Flores [a], Araceli Rodríguez [a], Roberto Ovilla [b], Gregorio Ignacio [c], Raquel Amador [c], Victor Salinas [d], Fernanda Perez [a], Danaee Rodríguez [a], Zoila Morales [a], Gonzalo Llinguin [a], Alejandra Vazquez [a], Analia Altamirano [a], Clara Gorodezky [a,*]

[a] *Department of Immunology and Immunogenetics, Instituto de Diagnóstico y Referencia Epidemiológicos-InDRE, Secretary of Health (SSA), Mexico City, Mexico*
[b] *Unit of Bone Marrow Transplantation, Hospital Angeles de Las Lomas, Mexico City, Mexico*
[c] *Service of Hematology, Hospital General Regional No 1. Gabriel Mancera, IMSS, Mexico City, Mexico*
[d] *Service of Onco-Hematology, Hospital Español, Mexico City, Mexico*

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Abstract

HSCT provides the opportunity to replace a damaged tissue. It is the most important treatment for high risk hematologic malignant and non malignant disorders. An important challenge in the identification of matched donors/patients is the HLA diversity. The Mexican Bone Marrow Registry (DONORMO) has nowadays >5000 donors. The prevalent alleles are Amerindian, Mediterranean (Semitic and Spanish genes) and African. In theory, it is possible to find 11% of 6/6 A–B–DR low resolution matches for 70% of patients with Mexican ancestry. We contributed with 39 unrelated, cord blood and autologous HSCT for patients with malignant, genetic and autoimmune disorders. Overall disease survival was 50% (2–7 years) depending on the initial diagnosis, conditioning, disease evolution or other factors. Clinical studies using autologous and unrelated HSC are performed on patients with refractory autoimmune diseases producing mixed results: mainly, T1D, RA, MS, SLE. Improvement has been observed in skin damage and quality of life in SLE and systemic sclerosis. Disease stabilization in 2/3 of MS patients. However, in RA and T1D, initial benefits have been followed by eventual relapse. With growing clinical experience and protocol improvement, treatment-related mortality is decreasing. Proof efficacy will be achieved by comparing HSCT with standard therapy in autoimmunity.

Keywords: Hematopoietic stem cell transplantation (HSCT); MHC; Autoimmune diseases (AD); Autologous; Allogeneic; Unrelated HSCT; HLA

* Corresponding author. Department of Immunology and Immunogenetics, InDRE, SSA, Carpio 470 1st Floor, Mexico City, D.F., 11340, Mexico. Tel.: +52 55 5341 4569, +52 55 5342 7557; fax: +52 55 5341 4418.
E-mail address: clarag@servidor.unam.mx (C. Gorodezky).

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1. Introduction

1.1. Overview

Immunology plays a central role in allogeneic HSCT. This treatment was developed as a strategy to prevent the bone-marrow toxicity that is caused by intense chemotherapy regimens and it cures a significant percentage of patients who have otherwise fatal hematologic malignancies. Reciprocal immune reactions between donor and recipient are a major feature of allogeneic HSCT and have both, deleterious (GVHD—graft versus host disease) and beneficial consequences (GVL—graft versus leukemia effect). Other immunological mechanisms involved in engraftment, control of malignancy, the development of tolerance and immune reconstitution requires understanding of the immunogenetic basis for immune reactions provoked by grafting tissue from one individual to another [1].

2. Major histocompatibility antigens

The Major Histocompatibility Complex (MHC) is the most important genetic region in the human genome in relation to infection, autoimmunity and transplantation. The HLA complex (Human Leukocyte Antigens)