Autologous Hematopoietic Stem Cell Transplantation in Hematological Malignancies

An Essay submitted for the partial fulfillment of The Master Degree in Clinical and Chemical Pathology By

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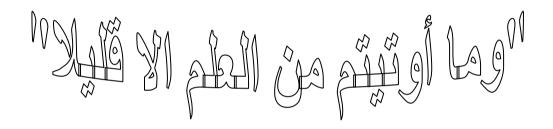
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Glossary

ACD-A Anticoagulant-citrate-dextrose, Formula A

AHSCT Autologous hematopoietic stem cell

transplantation

ALDH Aldehyde dehydrogenase

ALL Acute lymphoblastic leukemia
AML Acute myeloblastic leukemia

APC Antigen presenting cell

BM Bone marrow

BMT Bone marrow transplantation

CAM Cell adhesion molecule
CD Cluster of differentiation
CFC Colony-forming cell

CLL Chronic lymphocytic leukemiaCML Chronic myelocytic leukemia

CR Complete remission CXCR4 CXC receptor 4

DMSO dimethyle sulfaoxide

Flt3-L fms-like tyrosine kinase 3 ligand
 G.CFC Granulocyte colony forming cell
 G.CSF Granulocyte-colony stimulating factor
 GM.CFC Granulocyte-macrophage colony forming cell
 GM.CSF Granulocyte-macrophage colony-stimulating factor

GVHD Graft versus host disease

HD Hodgkin disease

HLA Human leukocyte antigensHSC Hematopoietic stem cell

HSCT Hematopoietic stem cell transplantation

IL InterleukinINF Interferon

LFA-1 Leukocyte Function-associated Antigen-1

Lin lineages (lin) markers

LTC Long-term culture

LTC-IC long term culture initiating cells
LVL Large volume leukapheresis

m- AB Monoclonal antibodies

MDS Myelodysblastic syndromeMHC Major histocontability complex

MIP-1 Macrophage inflammatory protein 1α

MM Multiple myloma

NHL Non hodgkin lymphoma

NOD/SCID Non-obese diabetic/severe combined

immunodeficient mice

PCR Polymerase chain reaction

PB Peripheral blood

PBPC Peripheral blood progenitor cell

PML/RARα Promyelocytic Leukemia/Retinoic Acid

Receptor- a

RBCs Red blood cells
Sca-1 Stem cell antigen
SCF Stem cell factor

SDF-1 Stromal drived factor-1

SRC Severe combined immunodeficient

repopulating cell

t- Translocation

TNH Tissue necrotizing factor

Thy-1 Thymocytes antigen

VCAM Vascular cell adhesion molecules

WBCs White blood cells

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INTRODUCTION AND AIM OF THE WORK

Introduction

Introduction

During the past two decades bone marrow transplantation has become a standard tool for the management of hematopoietic malignancies (Roy et al., 2000). Autologous bone marrow transplantation involves the use of patient's own hemopoietic progenitor cells to reestablish into mature blood lineage, such as leukocytes, platelets, erythrocytes after the administration of high-dose chemotherapy and/or radiation therapy (Fliedner, 1998).

The reinfused hematopoietic progenitors may come from the patient's marrow or more recently peripheral blood. Generally, before peripheral stem cell harvest, the stem cell content of the blood is augmented by treating the patient with chemotherapy and cytokines. Cytokines may decrease binding forces between stem cells and components of the stromal microenvironment, thus facilitating the migration of stem cells into the peripheral blood (Lapidot and Petit, 2001).

Most of the stem and progenitor cell compartment bear the cell surface antigen CD34. Enumeration of CD34 cells allows for more accurate assessment of engraftment potential provided by a given number of mononuclear cells, (Ronald et al., 2004). The Processing of stem cell is a cornerstone in success of transplantation process which includes isolation, and purification procedures (Kenneth et al., 2000).

Autologous stem cell transplantation has few post transfusion complications comparable to allogeneic stem cell transplantation. A concern related specifically to autologous transplantation is the possible presence of **Introduction** 2

contaminating tumor cells in the graft (**Ritchard**, 1999). A number of approaches have been employed to rid the graft off tumor cells, including purging tumor cells with antibody plus complement, or the use of peripheral stem cell techniques for both positive and negative purging to reduce tumor cell contamination (**Davood et al.**, 2001).

Autologous stem cell grafting has been used with varying degrees of success for hematopoietic malignancies (acute and chronic leukemia, Hodgkin's and non Hodgkin's disease multiple myeloma and myeloproliferative disorders). It can improve the duration of remission and provide a better quality of life (John et al., 2002).

Aim of the work

The aim of our essay is to review the general procedures of autologous hematopoietic stem cell transplantation and its role in the treatment of hematopoietic malignancies. Our objectives are to understand the basic concept of autologous stem cell transplantation and to build knowledge to enable an understanding of its future progression.

REVIEW OF LITERATURE

HEMATOPOIETIC STEM CELL (HSC)

INTRODUCTION

Throughout life, human own cells need to be replaced. The cells responsible for this normal turnover and repair are described as stem cells. A stem cell is the "mother cell" that leads to production of all various types of cells. The stem cells inside an embryo will eventually give rise to every cell, organ and tissue in the fetus's body, unlike other regular cells, that only can replicate to create more of its own kind of cells (**Petzer et al.**, 1996).

There are two types of stem cells: embryonic stem cells and adult stem cells. Embryonic stem cells come from an embryo. Embryonic stem cells form the mass of cells in the earliest stage of human development, which will eventually grow into a fetus. When the embryo is between three and five days old, it contains stem cells, which are busily working to create the various organs and tissues that will make up the fetus (**Tavian et al., 1996**).

Adults also have stem cells in the heart, brain, bone marrow; lungs and other organs. They are built-in repair kits, regenerating cells damaged by disease, injury and everyday wear and tear (**Tavian et al., 1996**).

A fundamental character of stem cells is the lasting ability to multiply when called upon to differentiate into specialized cells that can no longer divide (**Petzer et al., 1996**).