Hematopoietic Stem Cell Transplant for Mycosis Fungoides and Sézary Syndrome

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KEYWORDS

• Cutaneous T-cell lymphoma • Mycosis fungoides • Sézary syndrome
• Autologous hematopoietic stem cell transplant • Allogeneic hematopoietic stem cell transplant
• Myeloablative • Reduced-intensity conditioning

KEY POINTS

- Autologous transplant has low treatment-related complications in mycosis fungoides (MF)/Sézary syndrome (SS), but high relapse rates.
- Allogeneic transplant has curative potential in MF/SS with lower relapse rates and improved survival.
- Allogeneic transplant induces an immune-mediated graft-versus-lymphoma (GvL) effect in MF/SS.
- Myeloablative conditioning (MAC) in MF/SS is associated with higher risk of treatment-related toxicities and acute graft-versus-host disease (GVHD) and is limited to younger and medically fit patients.
- Reduced-intensity conditioning (RIC) in MF/SS shows lower treatment-related complications and is increasingly used in older patients with comorbidities.
- There is no difference in chronic GVHD between MAC and RIC.
- Relapses following allogeneic transplant respond to GvL effect induced by decreased immunosuppression and donor lymphocyte infusion (DLI).

INTRODUCTION

Primary cutaneous T-cell lymphomas (CTCL) represent a heterogeneous group of non–Hodgkin lymphomas (NHLs) that manifest in the skin with no evidence of extracutaneous disease at the time of diagnosis. The exception is MF, the most common type of CTCL, which accounts for more than 50% of primary cutaneous lymphomas.[1] MF is generally associated with an indolent course with most of the patients presenting in early stage of the disease. However, about one-third of

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patients present with advanced stage (generally considered to be stage IIB and higher) and another 25% progress into higher stage in the course of their disease.[1–3] SS is the leukemic and most commonly encountered type of aggressive CTCL.[1]

Most patients with early-stage MF respond well to skin-directed therapies with reported long-term remissions. Treatment for patients with advanced disease includes various combinations of skin-directed therapies, biologic response modifiers, histone deacetylase (HDAC) inhibitors, investigational agents, as well as single-agent and/or multiagent chemotherapy regimens.[4,5] None of these treatment options have been shown to prolong disease-specific survival or overall survival (OS) and often lead to short-term disease control with a median survival ranging from 1.4 to 4.7 years in patients with advanced stages (IIB–IVB) of MF and SS.[6] Borrowing from the paradigm of aggressive lymphomas, hematopoietic stem cell transplant (HSCT) has been explored as a treatment option in patients with advanced-stage MF/SS and other subtypes. The data for using high-dose therapy and autologous HSCT (ASCT) remain disappointing, but the results of allogeneic stem cell transplant are encouraging for the treatment of CTCL. The data series are small, and there is little consensus on conditioning regimens and other aspects of the transplants that are largely driven by institutional preferences. This article discusses the role of allogeneic stem cell transplant in the care of patients with CTCL and presents relevant data to support its use.

OVERVIEW OF HEMATOPOIETIC STEM CELL TRANSPLANT

HSCT, formerly known as bone marrow transplant (BMT), is a medical procedure in which multipotent stem cells derived from the bone marrow, peripheral blood, or umbilical cord are infused into a patient for treatment of hematological disorders and malignancies. This procedure requires that the patient's own hematopoietic and immune function be suppressed enough to accept the infused cells and allow homing of these cells to the marrow spaces and establishment of a donor-derived hematopoietic system in the host. This procedure can be accomplished either by chemotherapy alone or by combination of chemotherapy with radiation therapy called conditioning or preparative regimen given before stem cell infusion. The establishment of a donor-derived hematopoietic system requires some time during which the patient remains pancytopenic and entirely depends on supportive measures to prevent and treat the complication of pancytopenia as well as the conditioning regimen. The stem cells can be derived from the patient's own hematopoietic system (autologous) or from an HLA-matched donor (allogeneic) who can be a sibling (related) or a matched unrelated donor. Other sources now extend to haploidentical family members and cord blood stem cells and are discussed below. Major indications for stem cell transplant include hematologic malignancies such as leukemia, lymphoma, multiple myeloma, and other myeloproliferative disorders. According to the Center for International Blood and Marrow Transplant Research (CIBMTR) data, approximately 12,000 autologous and 8000 allogeneic transplants were performed in the year 2013 and the numbers are increasing.[7]

STEM CELL SOURCES

Hematopoietic stem cells express properties of multipotency and self-renewal and reside in bone marrow niches supported by cytokines and other microenvironmental factors. Human hematopoietic stem cells express CD34, CD38, CD90, CD133, CD105, CD45, and also c-kit (CD117), the receptor for stem cell factor, and these cells test negative for the markers that are used for the detection of lineage commitment. Historically, stem cell collection was performed in the operating room under general anesthesia using a large trocar to collect bone marrow from the pelvic bones in adults and long bones in children. This procedure has now given way to peripheral blood as a source of stem cells through a process called apheresis.[8] The peripheral blood stem cells can be mobilized into the circulation either by chemotherapy (in case of autologous collections) or by injections of hematopoietic growth factors, that is, granulocyte colony-stimulating factor supplemented by CXR4 inhibitors such as plexiafor,[9] and collected. Most autologous stem cells are cryopreserved in dimethyl sulfoxide before infusion in contrast to allogeneic stem cells that are usually infused fresh on the day of collection. Umbilical cord blood (UCB), which is rich in hematopoietic stem cells, can be cryopreserved and used in an appropriate patient. However, because a cord can yield only small amounts of blood (approximately 50 mL), a single cord can only provide adequate stem cells for a child or small adult. Generally, 2 UCB units need to be combined for adult transplants, and there is now a significant body of data to support the safety and efficacy of this approach.

DONOR SELECTION

HLA typing is required to match a donor and recipient for allogeneic stem cell transplants. The major

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