Despite excellent survival of marrow transplantation (BMT) in acquired severe aplastic anemia (SAA) using sibling donors, graft-versus-host disease (GVHD) continues to remain a major problem resulting in long-term complications and impaired quality of life. Between Aug 1989 and Aug 2004, 35 patients at our centre with acquired SAA underwent BMT from HLA-identical sibling donors using cyclophosphamide (CY) 50 mg/kg × 4 (days −5 to −2) and anti-CD52 MoAb 0.75–1 mg/kg BW as conditioning. Prior to 1999, rat derived anti-CD52 MoAb (Campath-1G) was used. We switched to humanised version of anti-CD52 MoAb (Alemtuzumab) when it became available in 1999. Median age at BMT was 17 yrs (range 4–46). Prior to BMT, 58% were heavily transfused (>50 transfusions) and 42% had previously failed ATG. Unmanipulated bone marrow was used as source of stem cells in all except one. GVHD prophylaxis was with cyclosporine (CSA) alone in 21 (60%) patients; 14 received anti-CD52 MoAb in addition to CSA. Eight patients had graft failure (primary, 4; secondary, 4) with a cumulative incidence of 23%. Graft failure was non-significantly higher in those receiving CSA and anti-CD52 MoAb as GVHD prophylaxis. No cases of graft failure are seen in 10 patients treated after 1999. The cumulative incidence of acute grade II-IV GVHD and chronic GVHD was 13% and 4%, respectively. None developed extensive chronic GVHD. Of the 19 recipients positive for cytomegalovirus (CMV), reactivation was seen in 5 (26%) with in 100 days. No cases of late CMV reactivation were observed. Six patients died of complications related to BMT at a median of 248 days (range 47–414). With a median follow-up of 59 months, the 5-year survival was 83% (95% C.I. 68–96). There was a non-significant trend towards improved survival in patients transplanted after 1995 (94% vs. 74%). Of the 29 survivors, serial chimerism studies were available on 20 and showed: 100% donor cells, 15; stable mixed chimerism with >85% donor cells, 3; and autologous recovery, 2. All survivors are transfusion-independent and have performance status of 100% except one who developed avascular necrosis. We conclude that the conditioning regimen containing CY and anti-CD52 MoAb is well tolerated and efficacious for acquired SAA using HLA-matched sibling donors. Based on the encouraging results of our study, further investigations are in progress evaluating the role of Alemtuzumab in the transplant protocols for AA using CSA alone as GVHD prophylaxis.

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IN VIVO SPATIAL AND TEMPORAL ANALYSES IN MICE REVEAL REDUNDANCY OF LYMPHOID TISSUES IN INDUCING ACUTE GVHD AFTER ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION

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Allogeneic hematopoietic cell transplantation is an effective therapy for the treatment of malignant and non-malignant disorders, and yet graft-versus-host disease (GVHD) remains a major obstacle. Given the dynamic changes in immune cell subsets and tissue organization, which occur in GVHD, localization and timing of critical immunological events in vivo may reveal basic pathogenic mechanisms of GVHD. We transplanted light-emitting luciferase transgenic allogeneic splenocytes, and non-invasively monitored their tissue distribution in living mice with major histocompatibility differences. Bioluminescence images were used to guide tissue selection for high-resolution analyses of cell subsets and tissue distribution. We demonstrated the sequential infiltration of lymph nodes, Peyers patches and spleen by donor derived $CD4^+$ T cells initially, followed by $CD8^+$ T cells, and an evolution of homing receptors that correlated with patterns of cell distribution. These data underline the important role of secondary lymphoid organs as sites for GVHD initiation. To determine whether there are instructive priming sites for specific cell migration to GVHD target organs such as gut, liver and skin we selectively interfered with the migration of donor T cells to lymphoid organs by administration of blocking antibodies to L-selectin and MAdCAM-1. Treated allogeneic recipients interfered with entry of allogeneic splenocytes into some secondary lymphoid tissues yet still developed GVHD. Similarly, allogeneic Peyer's patch deficient recipients manifested intestinal disease and succumbed to GVHD. These animals were generated by treatment with lymphotoxin-alpha-IgG fusion protein during embryonic development. In vivo imaging and detailed cellular analysis showed that remaining lymphoid tissues compensated for the lack of others. Of importance, T cells that lacked homing molecules for secondary lymphoid organs had alloreactive properties in vitro, yet did not cause GVHD in vivo. Transplantation of T cells with defined homing properties therefore appears to be a promising alternative in conferring protective immunity early after HCT without the risk of GVHD.

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CHOOSING THE PATIENT FOR AMBULATORY STEM CELL TRANSPLANTATION

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Introduction: Allogeneic non-myeloablative stem cell transplantation has been shown to reduce systemic toxicity and make possible the procedure in an ambulatory setting. **Objective:** To describe the characteristics of patients selected for an ambulatory stem cell transplant based on a non-myeloablative chemotherapeutic scheme. **Material and Methods:** Forty one patients were included (26 males and 15 females) with the following diagnoses: CML (12), CLL (2), ALL (5), AML (10), NHL (3), HL (1), MDS (3), AA (2), MM (1) and renal cell adenocarcinoma (1). Ages ranged between 8 and 61 years, with a mean of 36 years. Karnofsky scores in all patients were superior to 80. All patients tolerated oral feeding. Hemoglobin values ranged between 6.8 and 15.8 g/dl with a mean of 12 g/dl. Platelet counts ranged between 14.4×10^9/L and $1{,}200 \times 10^9$/L with a mean of 207.8×10^9/L. Serum creatinine ranged between 0.54 and 2 mg/dL with a mean of 0.9 mg/dL. **Results:** Twenty patients completed the transplant on a fully ambulatory setting basis. All had a Karnofsky scale value of 100. Mean values were 13 g/dl (hemoglobin), 218.5×10^9/L (platelets) and 0.9 g/dL (serum creatinine). Twenty-one patients began the transplant procedure on an ambulatory basis, but eventually required admission because of fever and/or mucositis (inpatient days ranged from 4 to 24 days). Karnofsky scores in these patients ranged between 80 and 100. Mean values from these patients were 10.9 g/dl (hemoglobin), 195.7×10^9/L (platelets) and 0.93 mg/dL (serum creatinine). **Conclusions:** Half of the patients admitted to the study completed successfully their stem cell transplantation procedure on an ambulatory setting. Factors related to this outcome were normal hematological values after the transplant and Karnofsky scores > 80. These values could predict with a high degree of probability whether or not a stem cell transplantation could be successfully performed in an ambulatory setting.

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THE HEMATOPOIETIC CELL TRANSPLANTATION DATABASE AT DBMHC

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The dbMHC www.ncbi.nih.gov/mhc is a public resource for the storage, display and analysis of MHC related genotype and clinical data. This resource has been developed at National Center for Bioinformatics (NCBI) through collaboration with the International Histocompatibility Working Group (IHWG). One module provides public access to data of the Hematopoietic Cell Transplantation project (HCT) of the IHWG. The HCT section of dbMHC is intended to serve the unmet need of the research and