— 165 —

Nonmyeloablative stem cell transplantation using fludarabine-based conditioning regimen (Preliminary results)

I Kim*[1], JY Jung[2], DH Lee[2], HH Song[2], MH Lee[1], S-S Yoon[2], CS Kim[1], S Park[1], BK Kim[2], NK Kim[2]
Department of Internal Medicine, Inha University College of Medicine[1], Incheon and
Department of Internal Medicine, Seoul National University College of Medicine[2], Seoul, Korea

The use of non-myeloablative stem cell transplantation (NST) has been on increase for the aim of reducing treatment related mortality (TRM) while preserving the graft versus malignancy effect. We report our experience in 12 patients (median age 38, male to female 6:6) who had chemorefractory malignancies, i.e., acute myeloid leukemia (AML) in 4, acute lymphoid leukemia (ALL) in 2, non-Hodgkin's lymphoma (NHL) in 2, multiple myeloma (MM) in 1, renal cell carcinoma in 2, and breast cancer in 1. Eligibility required contraindication to conventional allograft (prior allogeneic bone marrow transplant in 3, autologous bone marrow transplant in 2, old age in 3, major organ dysfunction in 2, and refractory solid cancer in 3). The patients with AML received fludarabine 30mg/m^2/day and cytarabine 2g/m^2/day for 5 consecutive days. The others were conditioned with fludarabine 30mg/m^2/day and cyclophosphamide 60mg/kg/day for 5 and 2 consecutive days respectively. Graft versus host disease (GVHD) prophylaxis consisted of cyclosporin A alone. Peripheral blood stem cells from HLA-identical sibling donors mobilized with G-CSF were given on days 0 and 1. The median number of CD34+ cells/kg infused was 3.3 (range 1.15-13.3). All patients achieved ANC over 500/uL on median day of 11 (range 8-17). Donor/recipient chimerism was determined monthly using VNTR and/or FISH analysis. Donor lymphocytes were given in case of persistent mixed chimerism and/or progression of malignancy. Major disease response was observed in 8 (67%), including 3/4 AML, 2/2 ALL (one Ph+ patient achieved and maintained molecular remission up to day 340+), 1/2 NHL, 1/1 MM, 1/1 breast cancer, and 0/2 renal cell carcinoma. Relapse was observed in 3/8. Toxicity was mild aside from acute GVHD (≥grade 2 in 33%). Until now, 4 died (2 of disease progression, 2 of acute GVHD) with a TRM of 17%. Delayed rejection occured in 5 (42%), but autologous recovery was prompt. These preliminary results show that NST is well-tolerated with a low risk of TRM even in previously heavily treated patients, although the long term effect on the survival duration remains to be elucidated.

— 166 —

Origin of mesenchymal stem cells after allogeneic hematopoietic stem cell transplantation

Hyeoung-Joon Kim*, Kyeoung-Sang Choi, Sang-Hee Cho, Ik-Joo Chung, Chan-Hun Nam, Je-Jung Lee
Department of Internal Medicine, Chonnam National University Medical School, Gwangju, Korea

Human bone marrow (BM) contains mesenchymal stem cells (MSC) that can differentiate into various cells of mesenchymal origin. It remains a matter of controversy whether donor-derived stromal cells are capable of engraftment following hematopoietic stem cell transplantation (HSCT). To determine if donor-derived stromal cells are transferred to the recipients of allogeneic HSCT, we investigated the characterization of MSC in 11 patients 1 to 8 years after sex mis-matched allogeneic HSCT. MSCs cultured from BM mononuclear cells (MNC) were performed morphologic studies, phenotypic analyses for several mouse monoclonal antibodies using flow cytometry, fluorescence in situ hybidization (FISH) probe analysis for X-chromosome, PCR analysis for microsatellite polymorphism, mixed lymphocyte reaction for allogenic CD3+ T cells using ^{3}(H)-methylthymidine. All patients had complete engraftment with donor-derived stem cells as shown by detection of donor type DNA in peripheral blood MNC. Following culture, MSC appeared morphologically spindle-shaped cells and phenotypically showed the expression of SH-2 and SH-4. However, the cells did not express the hematopoietic markers of CD34 or CD45. MSC showed the genotype of recipient completely using FISH or PCR analysis. MSC did not have allogeneic T-cell stimulatory capacities compared to those of dendritic cells used for other experiments. MSC isoloated from primary culture were capable of differentiating along osteogenic lineages. In conclusion, our study confirmed that MSC isolated from recipients of allogeneic HSCT are not of donor genotype despite of full hematopoietic engraftment with donor type. Donor cells do not contribute to reconstitue the marrow microenvironment.