Antithymocyte Globulin May Reduce Chronic Graft versus Host Disease in Patients Undergoing Unrelated Peripheral Stem Cell Transplantation

Over the past few years peripheral blood stem cells have been increasingly used instead of bone marrow for allografting patients with hematologic malignancies. Peripheral blood stem cell transplantation is associated with major advantages like a more rapid neutrophil and platelet recovery as well as a faster immune reconstitution. However, several reports have also shown a significant higher incidence of chronic graft versus host disease (GVHD), particularly of extensive type, which is attributed to a 10- to 20fold increase in the number of T cells in the apheresis product. Recent articles confirmed this observation [1–3].

Preliminary results indicate that antithymocyte globulin (ATG) as part of the pretransplant conditioning regimen is able to reduce the incidence of acute and chronic GVHD in patients undergoing related or unrelated allogeneic bone marrow transplantation for various hematologic malignancies [4–7]. Since unrelated peripheral blood stem cell grafts might bear an even higher risk of chronic GVHD, we incorporated rabbit anti-human T-lymphocyte globulin (ATG Fresenius, Munich, Germany) into our conditioning regimen. ATG was given at a daily dose of 20 mg/kg administered as a 4-hour-infusion on 4 consecutive days (days -4 through -1). Three patients transplanted with this regimen are evaluable for the assessment of chronic GVHD. Conditioning in these cases consisted of fractionated TBI (3×4 Gy) and cyclophosphamide (120 mg/kg), GVHD prophylaxis of cyclosporine A, and a short course of methotrexate in addition to ATG. In all patients the grafts were derived from HLA A-, B- and DR-identical unrelated healthy donors, the number of CD34+ peripheral blood stem cells was 6,3/kg b.w. in patient No. 1 and 4.4 and 19.3/kg b.w. in patients No. 2 and 3, respectively.

Patient No. 1 was a 23-year-old male Caucasian who was transplanted for refractory acute lymphoblastic leukemia (ALL). He never experienced acute or chronic GVHD, but relapsed 6 months after successful engraftment and expired despite donor lymphocyte infusion therapy. The second patient was a 42-year-old male Caucasian who was allografted with a one-locus C mismatch donor for Philadelphia-positive chronic myeloid leukemia in first chronic phase after a 1-year course

of interferon-alpha therapy. After an observation period of 395 days he is in molecular remission and showed only transient limited chronic GVHD of the skin related to discontinuation of cyclosporine A. Reinstitution of the drug was rapidly followed by complete resolution of the skin rash.

The third patient, a 48-year-old female Caucasian, has been allografted for acute myeloid leukemia in second complete remission. Chimerism studies by analysis of variable numbers of tandem repeats (=VNTR) show full donor hematopoiesis and after an observation period of 270 days she is in continued complete molecular remission and does not show any signs of either acute or chronic GVHD.

These 3 cases suggest that the addition of ATG to the conditioning regimen can modify GVHD in patients undergoing unrelated peripheral blood stem cell transplantation. However, it may be counterbalanced by a higher rate of relapses and infectious complications. Therefore, prospective randomized trials are warranted in order to determine the value of this novel approach.

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