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Immunoablation followed by autologous stem cell transplantation in refractory autoimmune diseases: clinical outcomes and immune reconstitution

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Abstract

High-dose immunosuppression and autologous hemopoietic stem cell transplantation (ASCT) has been proposed as an investigational therapy for patients with refractory autoimmune diseases (AD). We report the results of a single-center study of ASCT in 15 patients with refractory systemic lupus erythematosus (SLE), 7 patients with progressive multiple sclerosis (MS), 1 patient with autoimmune thrombocytopenia (ITP) relapsed after splenectomy, and 1 patient with pure red cell aplasia (PRCA) in our institution from 1998 to 2009.

Methods: Autologous HSC were collected from bone marrow (n=4) or mobilized from peripheral blood with either granulocyte colony-stimulating factor (G-CSF) (n=2) or Cy and G-CSF (n=18).

Results: Three SLE patients died due to transplant-related complications, 1 MS patient died due to t-AML 4 years after ASCT, 2 SLE and 1 PRCA patients died after 8, 7 and 2 years respectively due to relapses. At a median follow up of 54 (16–124) months 7 patients are in complete remission (4 SLE, 2 MS, 1 ITP). Three MS patients are in a stabilization phase, while 1 MS patient relapsed 5 years after ASCT. CR observed in SLE patients is accompanied by a disappearance of anti–ds DNA and ANA antibodies and an increasing number of CD4+CD45RA+ T cells, CD4+CD25+bright T cells and CD4+Foxp3+ cells. We also demonstrated the increase of CD4+ and CD8+ T cells in the S/G2M phase of the cell cycle until 1 year after ASCT.

Conclusion: ASCT in refractory AD can induce stable long-term remissions; however, the majority of patients relapse. The assessment of immune reconstitution can be important to understanding the mechanisms of self-tolerance re-establishment. International clinical trials would be required to clarify these questions.

Keywords: immunosuppression, autologous hematopoietic stem cell transplantation, lupus erythematosus, multiple sclerosis, autoimmune thrombocytopenia