Hematopoietic Stem Cell Transplantation for Thalassemia

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Abstract

Thalassemia is an autosomal recessive disorder associated with defective synthesis of the α- or β-chain of hemoglobin. For β-thalassemia major patients, therapeutic options are either monthly red cell transfusions and chelation therapy or allogeneic stem cell transplant. Stem cell transplant is the only curative approach and success is inversely correlated with the degree of iron overload and hepatic damage. Without transfusions, thalassemic patients have tremendous skeleton deformities, as well as hepatomegaly and splenomegaly due to expansion of the hematopoietic system with extramedullary hematopoiesis.

Allogeneic hematopoietic stem cell (HSC) transplantation (HSCT) in thalassemia has been a cornerstone in the development of HSCT. The rational basis of HSCT in thalassemia consists of substituting the thalassemic HSC bearing ineffective erythropoiesis with an allogeneic one capable of effective erythropoiesis. This cellular replacement therapy is not limited to the diseased erythropoietic component, but leads to the replacement of the entire hematopoietic system. Nevertheless, it is an efficient way to obtain a long-lasting, probably permanent, clinically effective correction of hemolytic anemia, thus avoiding transfusion requirements and associated complications .

The transplantation approach for a nonmalignant disease is much different from transplantation in malignancies. In the former setting, the detrimental immunologic proprieties [GVHD] of the engrafted HSC are not balanced by an antimalignancy effect. This characteristic must be always considered in determining the risk/benefit ratio and therapeutic decision such as the kind and intensity of the conditioning regimen, GVHD prophylaxis, source of HSC, and adoptive posttransplant therapies.

The Pesaro group developed a prognostic scheme to predict transplant outcome in patients younger than age 17. This prognostic scheme included three variables all related to iron burden: quality of chelation received for the entire life before transplantation; hepatomegaly; and the presence of liver fibrosis at pretransplant hepatic biopsy examination. These variables stratified patients into three groups based on them having none, or one/two, or all three of the risk factors. Overall survival and thalassemia-free survival were significantly different in the three groups: 94% and 87% in the low-risk group, 84% and 81% in the intermediate-risk group, and 70% and 58% in the high-risk group, respectively. The rate of rejection/thalassemia recurrence was much higher in thalassemic patients than in patients transplanted because of malignancies. Several factors have been invoked to explain this difference: massive pretransplant exposure to blood products, not having received any chemotherapy before transplant, expanded erythropoietic marrow, and possibly splenomegaly.

Key Words: Hematopoietic, Stem cell, Thalassemi.

Oral Presentation

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