Can Low-Dose TBI Help Overcome Previous Graft Failure? Second Hematopoietic Stem Cell Transplantation Using a Treosulfan-Based Conditioning Regimen in Pediatric β-Thalassemia Major

Aras Gürcan, Seda[1]; Aylan Gelen, Sema[2]; Bagısov, Damet[2]; Al Amoudi, Shahad[2]; Yalçın, Koray[2]

[1]Altunizade Acibadem Hospital, [2]Acibadem Altunizade Hospital

Background: Allogeneic hematopoietic stem cell transplantation (HSCT) is the only curative treatment for transfusion-dependent β-thalassemia major (TDT). Graft failure remains a major challenge, particularly in patients with significant iron overload. The optimal conditioning regimen for second HSCT has not been established. We evaluated the outcomes of three pediatric patients who underwent a second HSCT using a treosulfan-based conditioning regimen incorporating low-dose total body irradiation (TBI).

Methods: Three pediatric patients with TDT (8–15 years) underwent a second HSCT after secondary graft failure following their first transplantation. The interval between transplants ranged from 11 to 34 months. Pre-transplant evaluation included serum ferritin, cardiac and hepatic T2* MRI, panel reactive antibody (PRA), and donor-specific antibody (DSA) assessment. All patients had marked iron overload. Conditioning consisted of fludarabine, treosulfan, thiotepa, and low-dose TBI (200 cGy). Peripheral blood stem cells were obtained from matched sibling donors (n=2) or a 10/10 HLA-matched unrelated donor (n=1).

Results: All patients developed declining donor chimerism and recurrent transfusion dependence after the first HSCT despite post-transplant interventions. Neutrophil engraftment occurred on days +14 to +17, while platelet engraftment occurred on days +14 to +21 in two patients and was delayed in one. Complete donor chimerism (100%) was achieved in all patients and remained stable throughout follow-up. After a median follow-up of 7 months (range, 6.5–7), all patients remained transfusion independent. No recurrent graft failure, severe acute graft-versus-host disease, sinusoidal obstruction syndrome, or significant transplant-related organ toxicity was observed. Two patients experienced CMV reactivation, both successfully treated with antiviral therapy.

Conclusion: A treosulfan-based conditioning regimen incorporating low-dose TBI achieved durable donor engraftment and sustained complete donor chimerism after second HSCT in pediatric patients with TDT. These findings suggest that low-dose TBI may represent a promising salvage strategy for graft failure and warrant validation in larger multicenter studies.