Haploidentical Stem Cell Transplantation With TCR Alpha/Beta and CD19 Depletion in a Case of Unstable Hemoglobin Disease

Kumar, Karunakumar DNB[1]; Badiger, Shobha MD[1]; Damodar, Sharat DM[1]; Bhat, Sunil MD[1]

Transplantation: February 2018 - Volume 102 - Issue 2 - p e45–e46
doi: 10.1097/TP.0000000000001986
In Brief

Author Information

[1] Department of Hematology and Bone Marrow Transplant, Mazumdar Shaw Medical Center, Narayana Health, Bangalore, India.

Received 21 July 2017. Revision received 16 September 2017.

Accepted 23 September 2017.

The authors declare no funding or conflicts of interest.

K.K. participated in the concept designing and writing. S.B. participated in intellectual inputs. S.D. participated in the critical editing and intellectual inputs. S.B. participated in concept designing, critical editing, and final approval.

Correspondence: Sunil Bhat, MD, Pediatric Hematology and Oncology, Mazumdar Shaw Medical Centre, Narayana Health City, Bangalore 560099, India. (sunilbhat_9@hotmail.com).

Haploidentical Stem Cell Transplantation With TCR Alpha/Beta and CD19 Depletion in a Case of Unstable Hemoglobin Disease

Karunakumar Kumar, DNB,[1] Shobha Badiger, MD,[1] Sharat Damodar, DM,[1] and Sunil Bhat, MD[1]

Unstable hemoglobinopathies are rare variants of structural hemoglobin (Hb) disorders, present with variable clinical phenotype ranging from mild anemia to severe hemolytic anemia. Matched sibling and alternate donor allogenic hemopoietic stem cell transplants (HSCT) are well described in thalassemia and sickle cell anemia patients. To the best of our knowledge, HSCT has not been reported in unstable hemoglobinopathies. We report a case of successful haploidentical HSCT with T-cell receptor (TCR) alpha/beta and CD19 depletion in unstable hemoglobinopathy patient.

CASE PRESENTATION

A 2-month-old female child was evaluated for pallor, poor breast feeding, and was diagnosed to have hemolytic anemia. Her workup for thalassemia was negative. From then on, she was received regular blood transfusions every 45 days. She was reevaluated at 5 years of age and found to have unstable hemoglobinopathy. Genetic workup revealed heterozygous mutation in HBB gene exon 2, variant c.128T > T/C; p.Phe43Ser. In view of severe hemolytic phenotype she was planned for allogeneic HSCT. Because she did not have matched sibling and unrelated donor, she underwent haploidentical HSCT with myeloablative conditioning chemotherapy (Table 1). In view of high rejection risk total body irradiation was added to the conditioning, and rituximab was used for posttransplant lymphoproliferative disease prophylaxis. Mother was 5/10 allele match with the patient and used as donor. TCR alpha/beta and CD19 depletion (on Milteny Clinimacs device) was used for graft-versus-host disease (GVHD) prophylaxis with no additional pharmacological agent. Posttransplant, she had prompt engraftment at day 12 with 100% donor chimerism at day 30 which was sustained at 3, 6, and 12 months post-HSCT. Immune reconstitution was satisfactory at 6 months and 12 months post-HSCT. She developed grade 1 skin GVHD and cytomegalovirus activation which was fairly controlled. Patient continued to remain symptom-free till date, and she is doing well 21 months post-HSCT.

DISCUSSION

Hb abnormalities are the most frequent genetic disorder, affecting nearly 7.0% of the world population.[1] Unstable hemoglobinopathies are very heterogeneous group of disorders from both genetic and clinical point of view with autosomal dominant inheritance.[2] Patients experience very mild to life-threatening hemolytic anemia based on the type of variant. So far, nearly 150-Hb variants have been identified as unstable Hbs.[3] Currently, there are no proper guidelines or recommendations to treat these disorders because these are of wide range and with low prevalence. Mild cases require only supportive measures. Severe cases require regular blood transfusion and allogenic HSCT is the only curative option. The use of haploidentical donor in patients who do not have matched sibling donor is steadily increasing with improved outcomes.[4] Experience with HLA mismatched transplants in benign disorders are limited. Because HLA mismatched transplants have high rates of GVHD and graft failures, T-cell depletion methods have been used to improve overall survival of these patients with certain limitations.[5] Using T-cell, alpha-beta,

TABLE 1.

Conditioning chemotherapy and GVHD prophylaxis

Therapy	Drug regimen
Myeloablative conditioning regimen	Fludarabine 35 mg/m^2 per day for 4 days from day −9 to day −6. Busulphan 4.0 mg/kg for 4 days from day −9 to day −6. Cyclophosphamide 45 mg/kg for 4 days from day −5 to day −2. Rituximab 200 mg/m^2 on day −2 TBI 2 Gy on day −1.
GVHD prophylaxis	TCR alpha/beta and CD 19 depletion
Cell dose	CD34, 20.5 × 10^6/kg; TCR, α/β/kg = 0.04 × 10^6; TCR, γ/δ/kg = 1.77 × 10^6; CD19/kg = 0.07 × 10^6)

TBI, total body irradiation.

Received 21 July 2017. Revision received 16 September 2017.

Accepted 23 September 2017.

[1] Department of Hematology and Bone Marrow Transplant, Mazumdar Shaw Medical Center, Narayana Health, Bangalore, India.

The authors declare no funding or conflicts of interest.

K.K. participated in the concept designing and writing. S.B. participated in intellectual inputs. S.D. participated in the critical editing and intellectual inputs. S.B. participated in concept designing, critical editing, and final approval.

Correspondence: Sunil Bhat, MD, Pediatric Hematology and Oncology, Mazumdar Shaw Medical Centre, Narayana Health City, Bangalore 560099, India. (sunilbhat_9@hotmail.com).

ISSN: 0041-1337/18/10202-e45

DOI: 10.1097/TP.0000000000001986