



Haploidentical stem cell transplantation with post-transplant cyclophosphamide in leukocyte adhesion deficiency type 1: a case report

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Dear Editor,

Leukocyte adhesion deficiency type 1 (LAD-1) is a rare autosomal recessive primary immunodeficiency disease (PID) that results from defective expression of the beta-2 integrin, CD18, on immune cells and results in impaired leukocyte adhesion, egression, and migration [1]. Hematopoietic stem cell transplant (HSCT) is the only known curative approach for LAD-1 treatment [2]. In the absence of a matched related donor (MRD) and matched unrelated donor (MUD), haploidentical HSCT using T cell replete graft with post-transplant cyclophosphamide (PT-CY) is an emerging option for patients with both malignant and benign hematological conditions [3, 4]. We report here the successful haploidentical transplantation using T cell replete graft and PT-CY in a patient with LAD-1.

A 15-month-old female child was diagnosed with LAD-1 at the age of 3 months. She had poor weight gain and frequent admissions for sepsis. Her umbilical cord had separated at the 4 weeks of age. There was no family history of consanguinity and any history of recurrent infections in the family members. Evaluation revealed high leukocyte counts ($50,400/\text{mm}^3$) associated with neutrophilia. The flow cytometric analysis of peripheral blood neutrophils revealed the complete absence of CD18/CD11b and CD18/CD11c integrin proteins. The T and B lymphocytes and serum immunoglobulin assay were normal. Since no matched related and unrelated donors were available, haploidentical peripheral blood HSCT with unaffected 32 years old father as a donor, using T cell replete graft and PT-CY, was performed. There was a major blood group mismatch between donor and recipient. Donor specific

antibodies (DSA) by luminex were negative. Reduced intensity conditioning regimen consisting of intravenous fludarabine and treosulfan was used [5] as shown in Fig. 1. She was infused a cell dose of 10×10^6 CD34⁺/kg body weight and T cell dose in the graft was 2.4×10^8 /kg. Post-transplant in vivo T cell depletion was done by cyclophosphamide 50 mg/kg/day on days +3 and +4. From day +5, graft versus host disease (GVHD) prophylaxis comprising of cyclosporine and mycophenolate mofetil (MMF) was added. Neutrophil engraftment occurred on day +15 and platelet engraftment was achieved on day +19. The patient did not develop acute or chronic GVHD. On day +24 and day +90, molecular chimerism analysis on peripheral blood cells revealed complete stable donor chimerism and 100% expression of CD18/CD11b and CD18/CD11c on neutrophils. On day +45, she developed CMV re-activation which was managed with oral valganciclovir. On the last follow-up, she is 7 months post-transplant with normal blood counts, free of infection, and without GVHD. Her last immune reconstitution panel showed normal number of B and T cells for the age.

So far, 101 patients have undergone HSCT for LAD-1 [6] with transplant-related mortality being 19%. Of these, 22 patients underwent haploidentical transplant with mortality of 32% and 12 (55%) received at least 1 subsequent transplant. All these haploidentical HSCT were T cell depleted ex vivo. We have reported here a successful haploidentical HSCT in a LAD-1 patient using T cell replete graft and PT-CY without serotherapy. Neven B et al. have also reported successful haploidentical HSCT using PT-CY in one case of LAD-1 but they used myeloablative conditioning with serotherapy (Alemtuzumab/Rituximab) [7]. Avoiding serotherapy helps in clearing the virus with rapid T cell reconstitution after reduced intensity conditioning but is associated with higher incidence of acute GVHD [8]. T cell replete haploidentical HSCT with PT-CY appears to be a new attractive alternative in PID patients who have no matched donor and need urgent transplant before they succumb to infections. It might be a

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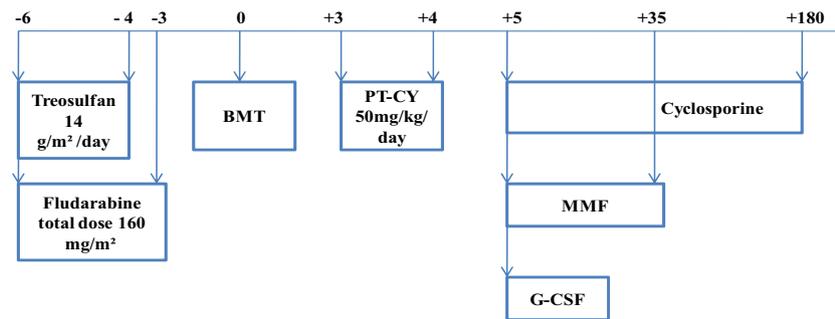


Fig. 1 Conditioning regimen and graft versus host disease prophylaxis. The child's weight was 8 kg. The intravenous treosulfan 14 g/m²/day was given over 3 days from day - 6 to day - 4. Fludarabine was given 40 mg/m²/day over 4 days from day - 6 to day - 3. Infusion (BMT) was done at day 0. Post-transplant cyclophosphamide (PT-CY) 50 mg/kg/day was

given on days + 3 and + 4. Cyclosporine was given from day + 5 to day + 180 post-transplant. Mycophenolate mofetil (MMF) was given at 30 mg/kg/day in three divided doses from day + 5 to day + 35. Granulocyte colony stimulating factor (G-CSF) 5 µg/kg/day was prescribed from day + 5 to day + 15

simple and widely applicable technique, avoiding the high cost of other procedures, including unrelated donor search, stem cell procurement, and ex vivo graft T depletion. Our case suggests that T cell replete haploidentical HSCT with PT-CY is a feasible curative option for LAD-1.

Compliance with ethical standards All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Conflict of interest None.

Informed consent Was obtained from the patient's parents in this study.

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