Immune reconstruction after allogeneic bone marrow transplantation in pediatric patients – experience of Fundeni Clinical Institute

Fundeni
Clinical Institute

Grigoraș O.¹, Serban C.¹, Gheorghe A.¹, Popa C.^{1,2}, Beldiman A.², Coliță A.^{1,2}

¹Center of Hematology and Bone Marrow Transplantation, Fundeni Clinical Institute, Bucharest, Romania;

²Department of Pediatrics–Fundeni Clinical Institute, University of Medicine and Pharmacy “Carol Davila”, Bucharest, Romania.

CONTEXT

Allogeneic hematopoietic stem cell transplantation (HSCT) has become a well-defined therapeutic strategy for a wide variety of malignant and non-malignant diseases with curative potential. Immune reconstitution post-HSCT is a complex and dynamic process, achieved in stages, depending on the type of transplant, the characteristics of the donor and the recipient, and the occurrence and stage of the graft versus host disease (GvHD). Innate immunity reestablished in the first months post-transplant, unlike adaptive immunity, that requires 1 to 2 years.

OBJECTIVE

The objective of our study is to identify the correlations between regenerating cell lineage and the time required for complete reconstitution of the immune status depending on the type of allogeneic transplantation.

DESIGN

We retrospectively evaluated 16 patients, who have been undergoing allogeneic transplantation between January 2015 and March 2018, and who survived at least 100 days after transplantation in the Pediatric Department, Fundeni Clinical Institute, Bucharest.

We analyzed the immune status (B, T and NK cells) by immunophenotyping, using the following markers: Lambda, Kappa, CD56, CD5, CD19, TCRgd/CD16, CD3, CD38, CD20, CD8, CD4, CD45 at well-defined checkpoint intervals (3 months, 6 months, 9 months, 12 months, and 24 months after the transplant).

Absolute values of each subgroup were calculated using the percentage of each subset and absolute count from the leukocytes. We also investigated the following viral infections after HSCT: CMV, EBV, BKV, and JCV.

RESULTS

In this study, the patients have been undergoing allogeneic HSCT transplantation for following malignant and non-malignant diseases: Acute lymphoblastic and Myeloid Leukemia (LAL, LAM), Juvenile Myelomonocytic Leukemia (JMML), Severe Aplastic Anemia (SAA), Fanconi Anemia (FA), Diamond-Blackfan Anemia (DBA).

The main demographic characteristics of the patients were: the boys/girls ratio is 1.6 (10/6), with an average age of 9.6 (range 1-18 years). 5 patients experienced immune recovery during the first 6 months, the NK cells subset has reconstituted in the first 3 months, and the last one to recover was the T cells subset (CD4+). In addition, we observed that the recovery of the CD8+ subgroup was between 6-9 months, while the CD4+ subgroup delayed recovery up to 2 years.

Immune status at 3 months and at 6 months

There were achieved 5 haploidentical HSCT, 8 HSTC from a matched unrelated donor (MUD), and 4 matched sibling donor (MSD). In our study group, the immune reconstitution rate was 20% for haploidentical transplantation, 37.5% for MUD and 25% for MSD. The average grafting period is the reconstitution of the polymorphonuclear leukocytes more than 500/ μ L in 2 consecutive days or more than 1000/ μ L.

Average grafting time depending on the type of transplant

In our study, the viral infections began in the post-grafting period, in the first 100 days after transplant, and could associate delayed in immune reconstruction.

Viral infections were present in approximately 50% of our patients independent of the type of transplant. CMV infection showed the highest frequency in our group, thus delaying NK-cells recovery from 3 months to 6 months.

CONCLUSIONS

In our center, patients undergoing transplantation from MSD have the fastest immune reconstitution. The immune reconstitution of patients after allogeneic HSCT influences long-term survival by contributing to the management of infectious complications and of GvHD.

REFERENCES

1. Wiegering V. et al, Pediatric Hematology Oncology Journal 2. 2017; 2-6.
2. Soghier L. et al, American Academy of Pediatrics. 2014; 5:94-96
3. Ogonek J. Et al, Frontiers in Immunology. 2016; 7:507