Successful Hematopoietic stem cell transplantation (HSCT) from matched unrelated donor (MUD) in a pediatric patient using myeloablative regimen suffering from MDS: A rare case report from western India

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Myelodysplastic syndrome (MDS) is characterized by heterogeneous hematopoietic stem cell disorders with ineffective erythropoiesis and dyserythropoiesis. Allogenic HSCT from siblings in our country in pediatric MDS is very well documented. But HSCT from matched unrelated donor (MUD) in pediatric age is still a new concept to implement in our country. We are here presenting the relapse case of MDS (Myelodysplastic syndrome) and we had done successful HSCT from MUD in a 14 year old pediatric patient. Myeloablative regimen (fludarabine, busulfan, cyclophosphamide, ATG) was used during HSCT. 100% donor chimerism was found on +day 34 VNTR study. Patient is doing well 1 year after HSCT without any complications.

Keywords: Allogenic matched unrelated donor (MUD); pediatric; MDS


Introduction

Myelodysplastic syndrome is a stem cell disorder; a rare entity in pediatric age group.[¹] Its clinical behavior is distinct in children as compared to adults. Allogenic HSCT from siblings in our country in pediatric MDS is very well documented. But HSCT from matched unrelated donor (MUD) is still a new concept to implement in the clinical practice.

Case Vignette

14 year old male patient presented with low grade fever and significant weight loss since 1 month. His past, personal and family history was not significant. His birth history was unremarkable. His complete blood count (CBC) shows pancytopenia. He underwent marrow aspiration and biopsy which showed hyper cellular marrow with dyserythropoiesis and megakaryopoiesis with 14% myeloblastic cells (Figure. 1). Diagnosis was made refractory anemia with excess blast-2 (RAEB-2). Immunophenotyping was positive for CD13, CD33, and CD117. Conventional cytogenetic showed trisomy 8 and FLT3 was negative. IPSS-R risk category suggestive of high risk (score 6).

He was started 3+7 induction (daunorubicin and cytarabine). Repeat marrow aspiration on post induction day +25 was in remission. Subsequently 3 cycles of high dose...
cytarabine (HIDAC) (3 gm/m2 cytarabine twice daily on d1, d3, d5) was given as consolidation treatment. Patient was put on observation. Patient developed weakness and giddiness after 6 months of observation. His CBC showed anemia and thrombocytopenia. Repeat marrow aspiration showed relapsed leukemic activity with 8% myeloblast, an occasional blast shows Auer rods.

As no sibling, his name was registered in national and international bone marrow donor registry. With waiting period of one month 10/10 matched donor was found. Patient was planned for allogenic HSCT from MUD. Donor was a 31 year old male patient and his blood group was AB positive. Patient’s blood group was B positive. He was given 3 cycle of decitabine as reinduction treatment before HSCT. Patient was in 2nd CR before HSCT. Double lumen Hickman catheter insertion was done by expert anesthetist. Pre HSCT work up was normal.

After taking written consent full myeloablative conditioning regimen (table1) was started. Source of donor stem cells were collected from the peripheral blood. On day 0 stem cells infused. (MNC: 7x10^9/kg, volume 160ml). Methotrexate was not given for acute GVHD prophylaxis. Patient had developed cyclosporine toxicity in the form of sudden weight gain and serum creatinine was 3.1mg% with high cyclosporine level. So cyclosporine was stopped and low dose of steroids started which is continued on discharge.

Antiviral, antifungal, PCP prophylaxis was given during HSCT procedure. 12 month after HSCT patient is under regular surveillance without any complications. We are gradually tapering cyclosporine and MMF (mycophenolate mofetil). Patient is in regular follow up with us.

**Discussion**

Myelodysplastic syndrome (MDS) is characterized by heterogeneous clonal hematopoietic disorders with ineffective erythropoiesis (lead to peripheral cytopenia) and immature hematopoietic cells (dyserythropoiesis) [2]. Pediatric MDS constituting 4% of all blood related malignancies of children. Its approximate annual incidence is 1-2 patients per million people in western countries [3]. Its incidence is not known in India. Because of scattered cases worldwide, pediatric MDS was included as childhood malignancies only in 2005. Pediatric MDS is different from adult MDS by its lower incidence, more constitutional abnormalities, more cytogenetic abnormalities, more aggressive clinically, absence of 5q deletion, rare occurrence of N-RAS mutation and more curative intent [2].

According to WHO classification our patient was in RAEB-2 type of MDS. It is defined by cytopenia(s), blasts (5%-19%), <1x10^9/L monocytes in blood and unilineage or multilineage dysplasia, Auer rods with or without blasts (10%-19%) in bone marrow. According to IPSS-R (revised international prognostic scoring system) patient was in HIGH risk category. Without treatment in this group of patients 25% of patients will develop AML within 17 months of duration and median survival is 19 months. Allogenic HSCT either matched or unmatched donor is the only viable curative option available to date for this group. Once determined for curative HSCT option, it is not always easy to complete it. As first setback is matching availability of HLA with siblings. If sibling is not available or HLA do not match then seeking unrelated donor from national and international donor registry is essential.

Recently new techniques of molecular HLA typing are available through which we can choose the truly matched 10/10 donor. This can prevent GVHD cases and survival rate being approached to HLA-matched sibling allogeneic HSCT. [4][5]Olle Ringdén et al concluded that no significant GVL effect happened in unrelated HSCT compare to HLA-identical sibling HSCT. Analysis by Daniel J. Weisdorf [6] showed better HLA matching can increase GVHD incidence and at the same time not prevent the chances of relapse so sibling donor is preferable.
Early upfront transplantation is recommended in children as curative intent as notable morbidity and mortality after conventional chemotherapy and high TRM. No role of intensive chemotherapy prior HSCT in children[7] European Working Group (EWOG) and EBMT (European bone marrow transplantation) study used myeloablative regimen comprising of melphalan, busulfan, cyclophosphamide patients shown DFS improvement in matched donor (87%) and matched unrelated (41%) [8]. Incorporation of busulfan in myeloablative regimen, shown by many large studied, leads to better outcome [9]. Due to risk of second malignancies and non inferior efficacy Total body irradiation (TBI) is not given nowadays. M Robin et al demonstrated similar outcome of reduced-intensity conditioning (RIC) regimen in 108 patients suffering from MDS/AML. These regimens are especially used in older patients and patients with co morbidity as tolerance is the main issue in that subset of patients. Performance status of our of patient is fair enough to receive myelo ablative regimen.[10]Increase incidence of chronic GVHD[11] if conditioning regimen is used without ATG in MUD type of HSCT.

Conclusion

Results of HSCT by MUD in pediatric MDS are nearly approaching towards related HSCT. Early allogenic HSCT gives better outcome. Awareness regarding national donor registry is also essential.

References