Editorials

Developments in Haematopoietic Stem Cell Transplantation

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Haematopoietic stem cell transplantation remains the treatment of choice for a variety of benign and malignant blood disorders.[1] In this modality Haematopoietic stem cell transplantation is the intravenous infusion of haematopoietic stem and progenitor cells to re-establish marrow function in patients with damaged or defective marrow. The procedure is called Bone Marrow Transplantation (BMT) if source of cells is Bone Marrow, Stem Cell Transplantation (SCT) if the cells are harvested from peripheral blood and Cord Blood Transplantation (CBT) if Placental / Cord Blood is infused as a source of rescue cells.[2]

BMT however remains the historical procedure and also the procedure which paved the way for the success of newer modalities of haematopoietic cell transplantation. It was in 1939 when the first patient was infused 18 ml of marrow from his brother for cure of aplastic anemia.[3] The subsequent identification of HLA antigens, development of cryobiology techniques and better understanding of human immune system lead BMT to a definitive form of therapy for many malignant and benign hematological disorders. The first successful BMT transplant was performed in late 1960s and the first successful autologous BMT was done in 1970s.[4,5] Since then BMT remained the sole modality of Haemotopoieties cell transplantation till mid 80s.

The concept of peripheral blood stem cell transplant is relatively new and its regular use started only in mid 1980s when major developments in mobilization, harvesting, preservation, colonogenic assays and identification of CD34 antigen were made possible.[6] It was in 1984 that the first patient with CML received chronic phase cells after myeloablative therapy for advanced disease.[7] The patient engrafted but relapsed. From mid 80s to mid 90s PBSCT were used with increasing success. In the year 2000-2001 greater than 90% auto-transplants and greater than 50% allo-transplants were of peripheral blood origin.[6,8] Clinical experience of over 10 years now confirms the superiority of PBSCT over BMT. This is largely because of significantly higher number of progenitor cells (CD34+cell/CFU-GM) in stem cell harvest achieved by leukapharesis. Also the number of candidate stem cells in the harvest (CD34+ CD38-, Thy -1+) is higher compared to BM harvest.[2,8] This results in faster, durable and complete engraftment which is translated into reduced morbidity, mortality and hospital stay costs. Also the immune reconstitution is faster and in allogenic setting the incidence and severity of acute graft versus host disease (GvHD) is no higher.[6] Additionally in allogenic setting there is enhanced graft vesus leukemia (GvL) effect and less chances of relapse have been reported compared to BMT. These favorable immune mediated effects are largely because of favorable subsets of T and NK cells and higher number of T cells present in stem cell harvest.[9] Furthermore peripheral blood stem cell harvest is feasible for gene therapy as majority stem and progenitor cells are in active state of cell cycle.[2,10]

Another advantage of PBSCT is that more donors are available for SCT compared to BMT. This is because the procedure is not painful, is without anesthesia and no admission is required. Also G-CSF is safe for mobilization and leukaphareis is not a fatal procedure and can be carried out on outpatient basis.[11]

The quest for allogenic donor however continued and cord blood emerged as a newer mode of transplantation in allogenic setting. This is a rapidly growing area because donor registries can provide matched donor to only 40% of the recipients, ethnic and racial minorities are under represented in these registries and time to find an unrelated donor is too long (4-5 months) which can be troublesome for patient and family.[12] Because of this reason cord blood banks are being established and a time may come when every body's cord blood will be cryopreserved for future use.

First CBT was performed in 1989 on a patient with Fanconia anemia.[13] By now more than 1000 CBT have been performed. The number of colony forming cells in CB (26,000/ml) is as great or greater than BM or SC harvest and these cells have higher self-renewal capacity.[14] T-cells in cord bood are much less allo-reactive therefore th incidence and severity of acute GvHD (Grade 2-4) is much less. For the same reason CBT are being performed with increasing success in sibling donors with 1-3 antigen mismatch and in unrelated donor setting with 1-2 antigen mismatch.[15] However, for reasons yet to be clear, hempoietic recovery with CBT is modestly delayed compared to SCT or BMT. Also it remains to be established if there are sufficient number of stem cells in CB to engraft an average sized adult since experience to date is mostly limited to children and small sized adults.[12]

The latest addition to Haemopoietic cell transplantation is non-myeloablative transplants (NSTs) also called mini-transplants. The idea of mini-transplants is basically derived from experience with donor lymphocyte infusion (DLI) in patients with leukemia relapsing after allo-BMT who have been induced to permanent remission after DLI.[16] Here the conditioning regimens are less myeloablative and highly immuno-suppressive.[17] Also post transplant immune-modulation is applied to prevent graft rejection and GvHD and to have enhanced GvL or graft versus malignancy (GvM) effect.[16,18] By now, more than 1,000 NSTs have been performed with increasing success. This is an exciting field since it has also been offered to older population where complications and deaths were found significantly less due to non-myeloablative nature of the conditioning regimen in NSTs. Alsomore mismatched related and unrelated donor

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Are we seeing the beginning of new era with the use of blood as the major source of haemotopoietic stem cells for transplantation? Certainly this seems possible.

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