



# Pediatric Hematology & Oncology RGCI & RC e-Newsletter

Rajiv Gandhi Cancer Institute & Research Centre, Delhi.

Issue 1; May 2009

## Editor's Message

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### Theme of issue

Hematopoietic stem  
cell transplantation  
in children

### In this issue

#### Editor's Message

Interesting case  
Relapsed Hodgkin  
disease is curable

#### Overview

Hematopoietic stem  
cell transplantation in  
children

It is a pleasure to launch the first issue of our e-newsletter in Pediatric hematology and oncology. It is being brought out with the aim of providing a forum for discussion of interesting cases and short review on current issues. We will appreciate contributions from all those involved in the care of children with hematological and oncological disorders.

This issue of our e-newsletter deals with a child with management of a child with relapsed Hodgkin's lymphoma and a current review on hematopoietic stem cell transplantation in children.

Pediatric hematology oncology has seen phenomenal progress in recent times. Research in stem cell transplantation in children is ongoing and has attained new heights. Hematopoietic stem cell transplantation has the capacity to achieve cure for many pediatric malignant and non-malignant diseases. Improved selection of donors using better HLA matching techniques, a wider selection of donor sources for unrelated transplants, newer regimens for immunosuppressive therapy and improved supportive care for complications related to the post transplant period have all led to improved outcomes.

In India there is a need for capacity building in terms of developing transplant centres to cope with the large number of patients who need HSCT as well as training transplant physicians and nurses.

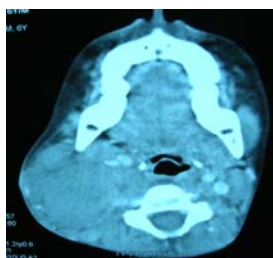
A brief overview of hematopoietic stem cell transplantation is provided in this issue. We also discuss an interesting case which signifies the importance of other modalities of treatment even after SCT.

Happy Reading!

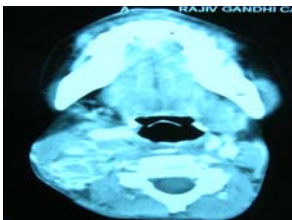
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## Radiotherapy may be essential component post stem cell transplantation in relapsed Hodgkin disease

*"He achieved complete remission after 2 cycles of ABVD"*



CT Neck at relapse



CT neck after 4 cycles of ICE

*"Received conditioning with BEAM. Stem cell (CD 34+ stem cell) dose infused was  $5.22 \times 10^6 / \text{cmm}$ "*

A 4 yr old male child was diagnosed with Hodgkin's Lymphoma, mixed cellularity, stage IA (Right cervical region) in summer of 2004. He was treated with ABVD based chemotherapy and achieved complete remission after 2 cycles. He went on to complete his treatment with 5 cycles of ABVD. No radiotherapy was given.

He remained well and on follow-up for 2 years when a right cervical node (1.5cm diameter) was noticed and proven to be relapse on biopsy.

The child was brought for further medical management about 7 months later (after having tried various forms of alternative therapies). Further investigations revealed it to be stage IIIA bulky disease.

Salvage chemotherapy with ICE (ifosphamide, carboplatin, etoposide) led to 40% regression after 4 cycles.

### Tumor Board Discussion (panel of multi-speciality experts):

*Question: What should be the further treatment strategy?*

*Expert opinion:* HL is a disease where even PR has survival advantage with autologous bone marrow transplantation

**Recommendation: Chemotherapy followed by autologous bone marrow transplantation**

*Question: What is the right time to do so?*

**Recommendation: Ideally, one would like to have the patient as close to CR as possible before starting conditioning.**

salvage regimes with Ifos/vinorelbine and Gemcitabine/Cisplatin achieving a partial response at best.

He then went on to receive conditioning with BEAM (BCNU, Melphalan, AraC, and VP16).

Peripheral blood stem cells (PBSCs) were harvested and supplemented with BM harvest as well (due to low CD34 count in PBSC).

Stem cells (CD 34+ stem cell dose-  $5.22 \times 10^6 / \text{cmm}$ ) were infused on D0 and child recovered from transplant without any major morbidity. Child went home after 3 weeks.

Post transplant evaluation revealed residual neck node of 2x2cm for which child received external beam RT to bilateral neck at 30.6 Gy/ x17 fractions. Post RT cervical lymph node showed complete regression and child continues to be well 7 months post transplant.

*The unique advantage of the Pediatric Hematology Oncology division of RGCI is the availability of multidisciplinary support from Pediatric oncosurgeon and radiotherapist in addition to the pediatric hematologist/ oncologist under the same roof.*

Patient went on to receive two more

## **Hematopoietic stem cell transplantation in children**

S Kaicker\*, G Kapoor

Hematopoietic stem cell transplantation has the capacity to achieve cure for many pediatric malignant and non-malignant diseases. Clinicians should be aware of current indications for stem cell transplantation and patients should be referred early to transplant centers. The field of bone marrow transplantation in India is undergoing dynamic change as more centres are taking up this challenging field.

The pediatric patient may often return to his hometown be cared for by his primary pediatrician after the initial months post transplant with frequent follow-up visits scheduled by the transplanting facility. It is therefore important that pediatricians taking care of such patients be aware of the possible late complications that can arise after transplantation.

In India, the number of children requiring bone marrow transplantation far exceeds the number of transplants that are actually being performed. The major limiting factor is the very high cost of transplantation (autologous transplant costs approximately Rs 3-6 lakh and allogeneic Rs 10-15 lakh with very few of these transplants being reimbursed by insurance). There are also limited centers with the expertise for performing transplantation and they may have a long waiting list for patients requiring transplantation. Setting up of national bone marrow registries and donor banks and drives in the community for voluntary marrow donation would be important steps to improve the availability of unrelated marrow sources.

Setting up of umbilical cord blood banks as a source of stem cells may also be an important way to expand the unrelated donor pool since this would not require voluntary donation. Moreover identifying and mobilizing sources of funding for patients with life threatening conditions where hematopoietic stem cell transplantation is the only curative option is another area that needs prioritization.

With the use of autologous transplantation the recipient's own stem cells are infused intravenously after treatment with myeloablative doses of chemotherapy.

The stem cells are typically collected early on in therapy (usually after the first 2-3 cycles of chemotherapy). They are stored with DMSO and frozen at  $-80^{\circ}\text{C}$  and can be thawed for use when required. Immuno-suppression is not required after autologous transplantation since the stem cells are the patient's own and there is no risk of graft versus host disease.

The common indications for autologous stem cell transplantation in children include Hematological malignancies (Hodgkin's Lymphoma- relapse or partial remission, Non Hodgkin's lymphoma- relapse or partial remission, AML and CML- investigational) and Solid tumors (Neuroblastoma stage IV, Ewing's sarcoma, PNET -metastatic\*, rhabdomyosarcoma\*, Wilms tumor\*, Germ cell tumor).

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*The pediatric patient may  
often return to his  
hometown be cared for by  
his primary pediatrician  
after the initial months post  
transplant*

*Stem cells are stored with  
DMSO and frozen at  $-80^{\circ}\text{C}$   
and can be thawed for  
use when required*

*For more details refer to  
Indian J Practical Pediatr  
2009; 11(2): 140-152.  
"Acknowledgement" to  
"Indian Journal of Practical  
Pediatrics"*

## Complications

*Chronic GVHD*

*Endocrine problems:*

*hypothyroidism,*

*hypogonadism, growth failure*

*Immunological*

*dysfunction Secondary*

*malignancies*

*Sterility, Cataracts,*

*Dental problems, Renal insufficiency*

*Cardiomyopathy,*

*Interstitial and*

*obstructive lung disease*

*Neuro-cognitive*

*problems manifesting*

*as school difficulties*

\*For solid tumors with metastatic disease at presentation or relapse that is sensitive to chemotherapy. Among solid tumors other than brain tumor and neuroblastoma, autologous transplant has not been shown to improve survival and remains an investigational modality of treatment.

## Allogeneic Hematopoietic stem cell transplantation in children

Allogeneic transplantation utilizes a stem cell source that is different from the patient's own stem cells. As mentioned above the donor of stem cells could be a twin, a sibling or an unrelated person. Hematopoietic stem cells for allogeneic transplants are currently available from 3 main sources: Bone marrow (BM), Peripheral blood stem cells (PBSCs) and (3) Umbilical cord blood (UCB) which is a rich source of hematopoietic stem cells. Traditionally, BM has been used as a source of stem cells for allogeneic HSCT and more recently PBSCs are gaining popularity.

Improved selection of donors using better HLA matching techniques, a wider selection of donor sources for unrelated transplants, newer regimens for immunosuppressive therapy and improved supportive care for complications related to the post transplant period have all led to improved outcomes.

The common indications Indications for Allogeneic transplantation in children include Non-malignant conditions (Hemoglobinopathies –thalassemia Mjor and sickle cell anemia, Immunodeficiency syndromes, Acquired aplastic anemia, Fanconi anemia, Diamond Blackfan anemia, Hemophagocytic lymphohistiocytosis) and Malignant conditions (Leukemias-AML, ALL, CML, JMML, Lymphoma- Hodgkin's and Non Hodgkin's in second remission, Myelodysplasia/myelofibrosis).

Bone marrow transplantation in malignant diseases (hematological malignancies and solid tumors) was designed initially with the goal of rescuing the recipient's marrow from the effects of myeloablative chemotherapy that was administered to destroy malignant cells. This was achieved by ablating the marrow with high dose chemotherapy alone or in combination with total body irradiation followed by intravenous infusion of hematopoietic stem cells. In the more recent past, the additional immune mediated effects of the donor allograft have begun to be recognized. Immune effector cells from the donor are thought to potentiate anti-tumor activity by creating a graft versus tumor effect.

### Points to remember

- Many diseases are potentially curable by bone marrow transplantation
- New techniques have reduced transplant related morbidity and mortality
- Gradually more centers have started doing BMT with good results

***We have been doing BMT routinely for the following indications : relapsed Hodgkin lymphoma, neuroblastoma stage 4 and thalassemia major***

*“Improved selection of donors using better HLA matching techniques, a wider selection of donor sources for unrelated transplants, newer regimens for immunosuppressive therapy and improved supportive care for complications related to the post transplant period have all led to improved outcomes”*

PHO e-newsletter RGCI & RC is edited by Dr Gauri Kapoor and published from the department of Pediatric Hematology/Oncology & BMT of Rajiv Gandhi Cancer Institute and Research Centre, sector 5, Delhi-110085.

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