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Non Cryopreserved Autologous Peripheral Blood Stem Cell Transplantation in Multiple Myeloma-Series of Cases in a Teaching Hospital in Eastern India

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ABSTRACT

Background: An autologous stem cell transplant is an established treatment option for patients with Multiple Myeloma. Many centers treat these patients and have transplantation capabilities but due to the high cost and lack of technical expertise lack of cryopreservation facilities for processing and preserving cells.

Methods: This retrospective study was conducted in IMS & SUM Hospital, Bhubaneswar, Odisha from August 2019 to January 2020 in which all the five cases of multiple myeloma which were eligible for stem cell transplant were included. Three stem cell transplants were performed in the COBE spectra auto PBSC system (Terumo BCT, Lakewood, CO) and rest two were performed in the Spectra Optia Apheresis system. Analysis of various characteristics like gender, age, weight, disease status, regimen used, pre-procedure total leukocyte count, pre-procedure CD34 positive cells count, pre-procedure absolute CD34+ cell count, mobilization regimen, time of harvest, and processed apheresis volume was done. All patients were followed until their engraftment and discharge.

Results: The number of days of stem cell harvest was 5th and 6th day. The median CD34 cell dose was 47.2/cells/µl. In all cases CD34 count in bag > 5 x 106/ kg .The median time to neutrophil engraftment was 10th day and platelet engraftment was 11th day in all cases. There were no adverse reactions during HPC transfusion. All patients were doing well till date.

Conclusion: Autologous Hematopoietic Stem Cell Transplant without cryopreservation resulted in adequate engraftment. Proper planning and coordination between clinicians and Transfusion Medicine specialist are a basic fundamental for efficient transplant and the best possible outcome.

Key Words: Multiple myeloma, Cryopreservation, Autologous Transplantation, Hematopoietic stem cell transplant, Engraftment

INTRODUCTION

An autologous transplantation can be performed with relative safety even in individuals in the late decades of life making its low mortality and moderate morbidity procedure. It is usually performed with the curative aim in individuals who have non-Hodgkin's lymphoma or Hodgkin's disease and patients who are suffering from multiple myeloma where the procedure is performed to prolong disease-free survival. Multiple myeloma accounts for 10% of all hematologic malignancies and 1% of all cancers.[1] n the patients who qualify for transplantation, high-dose chemotherapy followed by autologous hematopoietic stem cell transplantation becomes the lead therapy.[2] To begin with the therapy, these stem cells are to be mobilized from bone marrow to the peripheral blood with the use of chemotherapeutic drugs and growth factors such as Filgrastim (granulocyte colony-stimulating factor), Pegylated G-CSF, and Plerixafor (Mozobil) is given in patients who are poor mobilizers.[3] Stem cell collection by the process of leukapheresis is started when the CD34+ cell count in pe-

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ripheral blood is more than 10×10^6/kg body weight. Some studies show that this count should be more than 20×10^6/kg body weight.[4] It is generally accepted that the count of 2.0 to 3.0 $\times 10^6$ CD34+ cells/kg is essential to ensure hematological reconstitution.[5] However, these cases were studied to quantify the effects of autologous transplantation, in the centers which lack expensive cryopreservation facilities and technical expertise. As at our centre cryopreservation facilities are not available, so autologous stem cell therapy without cryopreservation was performed and remarkable results were observed. These case series emphasizes on engraftment and success of procedure followed by HSC transplantation without cryopreservation in resource constraint centers.

MATERIAL AND METHODS

Retrospective analysis of data was done in the Transfusion Medicine Department of IMS & SUM Hospital Bhubaneswar, Odisha, India from August 2019 to January 2020. During this time period, five cases of multiple myeloma, which were stem cell transplant eligible undergone stem cell transplant in the last 6 months, were included in the case series. Retrospective analysis of various characteristics like gender, age, weight, disease status, regimen used, pre-procedure total leukocyte count, pre-procedure CD34 positive cells count, pre-procedure absolute CD34+ cell count, mobilization regimen, time of harvest, and processed apheresis volume was done. Out of these five, three of them were performed in the COBE spectra auto PBSC system (Terumo BCT, Lakewood, CO), and rest two were performed in the Spectra Optia Apheresis system. After the procedure was completed, PBSCs were stored at 4-degree centigrade in our blood bank refrigerator for up to 72 hours and engraftment of neutrophil and platelet was observed.

RESULTS

During the study period, five patients with the diagnosis of multiple myeloma underwent autologous peripheral blood stem cell transplantation. Patients taken for this transplant were subjected to chemotherapy (7 cycles) and radiotherapy (6 cycles) in case 1 and rest were only taken for chemotherapy (6 cycles), for a period of 6 months. All of them underwent G-CSF induced mobilization for 5 days at 10mcg/kg in 2 divided doses. Plerixafor was also given in some cases. The collection was done on day 5. Details regarding CD34+ yield & median day of engraftment of neutrophil and platelets have been explained in **Table 1.**

Table 1: Detailed History and Outcome of Cases

S No	Parameters	Case 1	Case 2	Case 3	Case 4	Case 5
1.	Case History And Details	59/M Diagnosed as multiple myeloma (kappa LC disease) with Extramedullary plasmacytoma. Chemotherapy given for 6 months (7 cycles) & Radiotherapy (6 cycles)	55/M Diagnosed as multiple myeloma (IgG lambda). Chemotherapy given for 6 months (6 cycles)	52/M Diagnosed as multiple myeloma (IgA lambda). Chemotherapy given for 6 months (6 cycles)	50/F Known case of multiple myeloma (IgGkappa). Chemotherapy given for 6 months (6 cycles)	56/M Known case of multiple myeloma. Chemotherapy given for 6 months (6 cycles)
2.	Mobilization strategy	G-CSF Plerixafor	G-CSF Plerixafor	G-CSF	G-CSF	G-CSF Plerixafor
3.	Blood Volume Processed (ml)	14433	11628	14534	14005	11556
4.	CD 34+ Yield X10^6/kg	7.26	12.96	6.596	4.6	5.07
5.	Volume (ml)	257ml	260ml	259ml	252ml	282ml
6.	TNC X10^9/L	561.36	433.25	343.27	475.77	457.62
7.	Median day engraftment of platelet	11	11	15	11	13
8.	Median day of neutrophil engraftment	10	10	11	10	14

After the collection on day 5 with an adequate harvested product, the conditioning regimen was given the next day with high dose melphalan. PBSC infusion was started over a period of 35 to 45 minutes. Patients tolerated the infusion well and no adverse events were noted during and post-infusion.

The post-transplant course was managed with vigilant vitals, I/O monitoring, weight monitoring.

The time to neutrophil and platelet engraftment correlates with the CD34 cell number. Engraftment of both neutrophils and platelets was recorded and were found to be in the range of 10 to 15 days as shown in **Figure 1**.

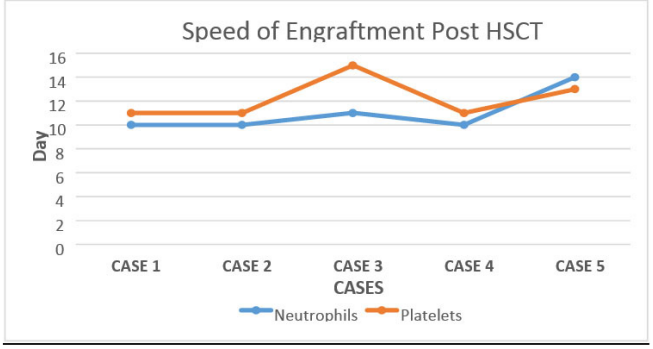

Figure 1: Engraftment of Neutrophils and Platelets Post HSCT.

Post-transplant transfusion requirement varied in all the 5 cases as described in **Figure 2**.

In case 1, the transfusion requirement was seven units of SDP, one unit of PRBC, and twelve units of FFP, whereas in cases 2 & 3, four units of SDP each were utilized. The requirement of SDP in case 4 was least with one unit only but two units of PRBC and three units of FFP were used.

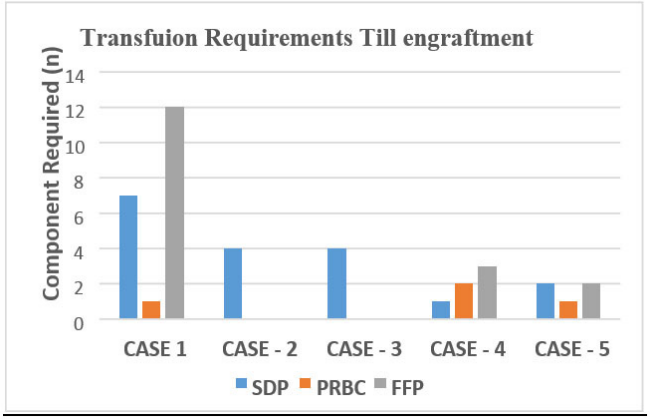

Figure 2: Number of Blood Components Utilized Post HSCT.

All five cases had undergone non-cryopreserved autologous peripheral blood stem cell transplantation, so all of them had tolerated the infusion well and the median time of engraftment was found to be within 10 to15 days.

DISCUSSION

Non-cryopreserved peripheral blood stem cell transplantation in multiple myeloma patients can be successfully performed in treating hospitals where there are no preservation facilities, but are well equipped to handle the ongoing crisis. In our study, it has been observed that there are many factors that determine the adequate yield of stem cell collection which includes age at diagnosis and vital stability of the patient, presence of underlying illness, past history of therapeutic therapies, the marrow store, time of initiation of stem cell therapy, the mobilization agents used and the equipment used for leukapheresis sessions. The patient receives high dose chemotherapy before transfusion until then these stem cells can be stored safely for 5 days at 2°C to 6°C.[6] Henceforth, these cells start losing their viability progressively. Alternatively, these cells can be preserved in blood bank refrigerators. Clinical Studies since the late 1950's show evidence in support of the use of non-cryopreserved stem cell collection stored for 2 to 9 days in patients receiving myeloablative drugs. This type of non-cryopreservation can be successful if provided with 2 conditions that are either that centre should be fully equipped to treat hematologic malignancies and lack cryopreservation facilities or in the department which are treating blood malignancies, with the ongoing process of establishing transplant facilities that will eventually have the capacity to establish cryopreservation at their centre. Non-cryopreserved stem cells have shown promising results with advantages; can be performed at daycares, are cost-effective, needless processing time, number of centres starting transplant have increased, DMSO toxicity is excluded, time-saving and viability is maintained.[7] The disadvantages for the same include the use of chemotherapeutic regimens employed are not standardized, team coordination is lacking regarding the timing of mobilization of stem cells, initiation of leukapheresis, administration and infusion of chemotherapeutic agents and stem cells respectively. Also, lack of proper storage facilities in cases where a good stem cell yield is obtained for tandem transplants. Studies show no difference in stem cell viability, no delay in engraftment of neutrophil and platelet, and long-term consequence of the primary disease.[8] Non-cryopreserved stem cell transplantation is safe, cost-effective, and can be established in hospitals that are well equipped regardless of cryopreservation facilities.[9]

CONCLUSION

To conclude, autologous Hematopoietic Stem Cell Transplantation can be successful in the centers with no

cryopreservation facilities and the results of engraftment are satisfactory. All the cases with multiple myeloma and who had undergone this transplant had shown adequate engraftment. The key to efficient transplant and the best possible outcome is the planning and coordination between clinicians and Transfusion Medicine specialist.

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Ethical Clearance: As we have done retrospective analysis of departmental data there is no requirement of ethical clearance.

Conflicts of interest: There are no conflicts of interest.

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