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Preliminary Observation on the Influence of Tumor Osseous Metastasis on Autologous Peripheral Blood Stem Cell Collection

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OBJECTIVE To examine the influence of tumor osseous metastasis on the patients undergoing autologous peripheral blood stem cell collection.
METHODS A total of 36 patients with malignant diseases who received an autologous peripheral blood stem cell transplantation, during a period from April 2004 to June 2006, were chosen. The patients were divided into two groups, i.e. group A were patients with a complication of tumor osseous metastasis, and group B were without metastasis. Both groups were treated with Taxotere 120 mg/m^2 plus granulocyte colony-stimulating factor (G-CSF) 5 μg/kg/d, for a mobilization regimen. A blood cell separator was used to collect the mononuclear cells. The proportion of harvested CD34+ cells in the peripheral blood and the collected mononuclear cells were detected by flow cytometry. The number of CD34+ cells was used to determine the difference in the nature of the collections between the two groups.
RESULTS After mobilization in groups A and B, the number of the peripheral blood mononuclear cells (PBMC) was 39.3 ± 14.7% and 41.1 ± 12.4 % and the proportion of CD34 + cells was 0.16 ± 0.07% and 0.17 ± 0.10%, respectively. Following administration of the drugs, there was no significant difference between the number of harvested PBMC and CD34+ cells of the two groups, i.e., 3.47 ± 1.16 × 10^8/Kg and 2.52 ± 1.43 × 10^6/Kg in group A and 4.02 ± 1.31 × 10^8/Kg and 2.73 ± 1.87 × 10^6/Kg in group B, respectively.
CONCLUSION Osseous metastasis, as a single factor, may have no impact on mobilization and harvesting of hematopoietic stem cells and their engraftment after autotransplantation.

KEYWORDS: osseous matastasis, autologous peripheral-blood stem cell transplantation, harvest

Since 1990s, autogeneic hematopoietic stem cell transplantation (Auto-HSCT) has been rapidly developed. It has replaced or is replacing the methods of heterogenic hematopoietic stem cell transplantation such as bone marrow transplantation etc. and in some clinical fields it is extensively used for the treatment of various malignant diseases[1]. Besides malignant tumors of the hematopoietic system such as leukemia etc, Auto-HSCT therapy also has been used for many solid tumors, i.e. lymphoma, testiculoma, non-small cell lung cancer, osteosarcoma, breast cancer and ovarian cancer etc, as well as benign diseases, such as a regenerative anemia, autoallergic diseases and connective tissue diseases etc.[2-10]. The quality of stem cell harvesting is directly related to the success or failure of the transplantation treatment and quality of the harvest may also relate to other conditions. For instance, osseous metastasis may occur from a solid tumor, and the tumor cells can mix with the bone marrow, and form a new tumor focus[11,12]. Growth of the metastatic tumor cells may suppress the

hemopoietic microenvironment of the bone marrow, which is bound to produce a definite effect for growth and proliferation of the hemopoietic stem cells. It is unknown whether or not osseous metastasis will effect the quality of peripheral blood stem cells harvested following mobilization. The quality of stem cell harvests for patients with or without the concurrent osseous metastasis from a tumor have been examined and the analysis reported as follows.

MATERIALS AND METHODS

Case information

A total of 36 tumor patients, 21 male and 15 female patients with a mean age of 51.4 years, who agreed to receive an Auto-HSCT during the period from April 2004 to June 2006, were selected. They were divided into two groups, i.e. 11 cases in Group A having concurrent osseous metastasis, comprised of 4 male and 7 female patients with a mean age of 45.3 years. Group B consisted of 25 cases without osseous metastasis, made up of 11 male and 14 female patients. No severe functional disturbance of the organs was found in any patients, and the PS scoring was less than 2.

Mobilization and harvesting of the hemopoietic stem cells

Taxotere monochemotherapy (120mg/m^2) plus G-CSF 5 μg/Kg/d was used tomobilize stem cells into the peripheral blood. Nine days after Taxotere treatment, the peripheral white blood cells (PWBCs) were less than 1.0 x 10^9/L. A successive GSF regimen was employed, with a dose of 5 ug/Kg/d, until the PWBCs were more than 3.0 x 10^9/L. MCS plus a PWBC cell detachment segregator was used for harvesting stem cells and a boost GSF was conducted before harvesting.

Two harvests were performed for each patient over two successive days. A blood routine assay was implemented for the harvested stem cells to determine the total white cell count and a percentage of the mononuclear cells. Cytometry was used to detect the percentage of the CD34 + cells. After obtaining the patient's body weight (BW) and estimation of the amount of the cell culture fluids, the numerical value of mononuclear cells and CD+34 cells per kg BW in the cell culture fluids was calculated, after statistical treatment.

Statistical treatment

SSPS 10.0 statistical software was used for analysis.

RESULTS

Although the number of mononuclear cells and CD34+ cell population in group B was, after the mobilization, higher compared to group A with complicated osseous metastasis of a tumor, statistical tests showed that there was no significant difference between the two groups in the mononuclear cells of the harvest and CD34+ cell population (Table 1).

DISCUSSION

Bone and bone marrow are the major sites for metastasis from malignant tumors of the breast, lung and prostate, etc. Osseous metastases from a tumor mainly occur in flat bones and the metaphysis of long bones. Most of the metastases are multiple metastases.

Hemopoietic stem cells (HSCs) are primary multidirectional potential cells, which have the ability to differentiate into various mature hematopoietic cells[13]. HSCs are mainly situated in the bone medullary stroma, and generally only a few can be found in the peripheral blood. However, they can proliferate after a patient receives chemotherapy and / or G-CSF, with a 2 or 10-fold increase in the peripheral blood. Enough HSC can be seceded and harvested by the blood cell separator, which can meet the needs of the transplant treatment. The Auto-HSCT has some advantages such as convenience, a lack of HLA restriction and graft versus host reaction etc.

Table 1. Comparison between the MNC and CD34+ cell populations in the peripheral blood and cell cul ture fluid.

Group	Peripheral blood		Cell culture fluids	
	MNC(%)	CD34+(%)	MNC(×108/kg)	CD34+(×108/kg)
A	39.3±14.7	0.16±0.07	3.47±1.16	2.52±1.43
B	41.1±12.4	0.17±0.10	4.02±1.31	2.73±1.87

* P>0.05.

However, with multiple osseous metastases from advanced malignant solid tumors, there is a suppression of the local hemopoietic microenvironment and a disruption of the growth and differentiation of the hemopoietic stem cells, impacting the Auto-HSCT. A study by Nieto et al.[14] has demonstrated that osseous metastasis can be an independent factor, directly relating to adulteration of the stem cell harvests, and contamination of tumor cells in the transplants might be a factor for recurrence and unfavorable prognosis.

At present, there are disagreements as to whether or not tumor cells have been included in the mobilization during stem cell harvesting, and there are questions relating to the effects of the tumor cells in the harvests on the prognosis, etc[15-17].

As a part of our study, we have observed the effect of chemotherapy plus G-CSF on mobilization for 36 solid-tumor patients receiving Auto-HSCT. The results showed that the number and quality of mononuclear cells and CD34+ cells mobilized during harvesting in the group without osseous metastasis were all slightly higher than that in the group with osseous metastasis, but there was no significant difference between the two groups, suggesting that osseous metastasis may have no apparent influence on the mobilization process and quality of the Auto-HSCT. The correlation factors such as past chemotherapy etc. have not been ruled out because of the small number of cases enrolled in the groups, so further studies are needed to resolve these issues.

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