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Risk factors for a poor hematopoietic stem cell mobilization

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ABSTRACT

Poor mobilization is an important problem in autologous stem cell transplantation. We retrospectively reviewed the data of 165 mobilized patients to identify possible risk factors for a poor stem cell mobilization. 27 patients (16.4%) were categorized as poorly mobilized. The poor mobilization ratio differed according to diagnosis (lymphoma: 25.4%, acute leukemia: 15.4%, amyloidosis: 14.3%, and multiple myeloma: 9.6%). Being diagnosed as lymphoma (odds ratio [OR] = 6.02, $p = 0.001$), advanced age (OR = 1.05, $p = 0.007$) and increased weight (OR = 1.03, $p = 0.03$) were found as possible risk factors. Being diagnosed as lymphoma was shown to be the most important risk factor for a poor mobilization. Leukapheresis staff should be aware of the increased risk of a poor mobilization in lymphoma patients and remobilization methods should be considered from the beginning.

1. Introduction

High dose chemotherapy followed by autologous stem cell rescue is one of the treatment alternatives for many malignancies [1–3]. Peripheral blood stem cells are mostly used as the source of stem cells due to the improvements in mobilization methods (cytokine with or without disease specific chemotherapeutic agents) and technical devices in leukapheresis. Since the source is the peripheral blood, the mobilization step is critical.

The success of a stem cell mobilization may be influenced by different factors (prior chemotherapy courses, the use of platinum compounds and alkylating agents, CD34+ cell adhesion molecule profiles or G-CSF doses, radiation therapy). Varying rates (5–46%) for poor mobilization have been reported [4–11]. Although there are alternative medications such as plerixafor [10,12], it is more expensive and its use and back payment is restrained by the reimbursement companies in various countries. Therefore, identification of risk factors for a poor mobilization is important for optimal resource utilization.

Based on these circumstances, foreseeing poor mobilization from the beginning is increasingly becoming an issue. In this study, we retrospectively evaluated possible risk factors for poor the stem cell mobilization using the data of our mobilized patients over a 14 year period.

2. Patients and methods

2.1. Patients

We retrospectively reviewed 165 patients who have been mobilized between 1998 and 2011. Data of patients (diagnosis, age, sex and weight, circulating CD34+ cell count, and total number of collected CD34+ cells) were obtained from the records of the hematology and immunology clinics. The study subjects consisted of patients with multiple myeloma ($n = 73$), lymphoma ($n = 59$), acute leukemia ($n = 26$), amyloidosis ($n = 7$). The characteristics of patients have been presented in Table 1.

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Table 1
The clinical features and characteristics of the patients.

	All patients	Good mobilizing patients	Poor mobilizing patients
Number of patients	165	*138*	*27*
Age (median, range)	*52 (19–75)*	*51 (19–75)*	*54 (22–68)*
Gender (male/female)	83/82	*70/68*	*13/14*
Diagnosis			
Multiple myeloma	73	66	7
Lymphoma	59	44	15
Acute leukemia	26	22	4
Amyloidosis	7	6	1
Number of chemotherapy cycles	*3 (1–8)*	*2 (1–8)*	*2 (1–5)*
Prior radiotherapy	*16 (9.7%)*	*13 (9.4%)*	*3 (11.1%)*
Refractory disease	*5*	*5*	*None*
CD34+ cells ($\times 10^6$/kg, median, range)	5.32 (0.28–110.7)	*6.1 (2.51–110.7)*	*1.6 (0.28–2.4)*
Weight (kg, median, range)	70 (40–134)	*70 (40–134)*	*75 (53–130)*
Number of apheresis (median, range)	3 (1–8)	*2 (1–6)*	*4 (1–8)*

2.2. Previous therapies

In patients with amyloidosis and multiple myeloma, vincristine, adriamycin and dexamethasone (VAD) with or without bortezomib were administered as the initial therapy. Cytarabine for 7 days and idarubicine for 3 days were administered to the patients with acute myeloid leukemia as the induction therapy. In patients with acute lymphoblastic leukemia, the Hoelzer protocol ± prophylactic cranial irradiation was used as the induction therapy.

In patients with non-Hodgkin lymphoma, the cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) ± rituximab were administered as the first line treatment. In patients with Hodgkin lymphoma the doxorubicin, bleomycin, vinblastine, and dacarbazine (ABV-D) ± involved field radiation therapy were administered as the initial therapy. In all lymphoma patients, methylprednisolone, cisplatin and cytarabine (ESHAP) or ifosfamide, carboplatin and etoposide (ICE) regimens were administered as the relapsed or refractory therapy.

2.3. PBSC mobilization

A mobilization was performed by administering G-CSF (10 μg/kg/day, mostly filgrastim) with or without disease specific chemotherapies (ESHAP or ICE for lymphoma patients, high dose AraC for acute leukemia patients and cyclophosphamide for multiple myeloma patients). In the patients receiving G-CSF and chemotherapy, an apheresis was initiated when the circulating CD34+ cell count was higher than 10 cells/μL. In the patients receiving only G-CSF, an apheresis was initiated on the 5th day.

2.4. Collection of peripheral blood stem cells

A leukapheresis was performed by using various types of automated apheresis systems (Comtec/Astec 204, Fresenius, Waltham, MA; Model CS3000 plus, Baxter Fenwal, Lake Zurich, IL; COBE Spectra [Version 5.1 – 6.0], GambroBCT, Lakewood, CO; excel pro, Dideco, Mirandola). Among the 46 patients who underwent leukapheresis, the median leukapheresis number was 3 (range, 1–8). In the five patients with significantly low (5 cells/μL) PBCD34+ counts, an apheresis was not initiated.

Mobilization insufficiency was defined as the peripheral blood CD34+ cell count less than 10/μL during the post-mobilization period or total collected CD34+ cell count less than 2.5×10^6/kg with six apheresis.

2.5. CD34+ counts

The number of CD34+ cells was counted by a flow cytometer (BD FACSCalibur, BD Biosciences, 2003, USA). All of the samples were analyzed with the BD Procount Progenitor Cell Enumeration kit (Catalog No.: 340498, BD Biosciences).

2.6. Statistical analysis

We analyzed the relationship between mobilization and different variables (age, weight, sex, and diagnosis of patient) by the multivariate test (logistic regression). p Values less than 0.05 were considered as significant. The data were analyzed using computer software (SPSS 16.0, SPPS, Inc., Chicago, IL).

3. Results

The patients were composed of 83 males and 82 females. Their median age was 52 (range, 19–75) years old and the median weight was 70 kg (range, 40–134 kg). The median number of apheresis per patient was 3 (range, 1–8). A total of 457 procedures were performed in 159 patients. The median of collected CD34+ cells was 5.3×10^6/kg (range, 0.28–110.7 $\times 10^6$/kg; Table 1).

A poor mobilization was documented in 27 (16.4%) patients (Table 1). According to the total number of collected CD34+ cells (between 2.5 and 5×10^6/kg vs. more than 5×10^6/kg), successfully mobilized patients were divided into two groups. The number of the patients in each group was 42 (27.4%) and 92 (56%), respectively (Table 2).

Poorly mobilized seven patients were remobilized with G-CSF or chemotherapy plus G-CSF. Two of them (28%) with the diagnosis of multiple myeloma could be mobilized at the second attempt. Two patients were tried to

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