CORRESPONDENCE

Peripheral Blood Monocyte Count is a Predictor of Successful Peripheral Blood Stem Cell Harvest After Chemo-Mobilization in Patients with Malignant Lymphoma

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High-dose therapy (HDT) followed by autologous hematopoietic stem cell transplantation (ASCT) is useful for patients with chemosensitive refractory/relapsed non-Hodgkin lymphoma, Hodgkin lymphoma, or newly diagnosed mantle cell lymphoma (MCL). For successful ASCT, infusion of an adequate number of CD34 positive cells is important. However, the best strategy for harvesting peripheral blood stem cells (PBSCs) and the factors correlated with effective mobilization are still unknown. Here, we retrospectively analyzed the factors correlated with optimal PBSCs mobilization.

Between November 2006 and December 2015, 36 patients diagnosed with malignant lymphoma underwent harvesting of PBSCs at Yokohama City University Medical Center. They were judged as suitable for HDT followed by ASCT. PBSCs were mobilized using chemotherapy followed by G-CSF (lenograstim and filgrastim) or G-CSF alone at the physician's discretion. We aimed to obtain $2.0 \times 10^6/\text{kg}$ CD34 positive cells in total. All patients received G-CSF approximately 5 days before mobilization until the last apheresis. Statistical analysis was performed with EZR software (version 1.32) [1].

There were 19 men and 17 women with a median age of 58 years (range 26–67 years). Of 36 patients, 18 (50%) were diagnosed with diffuse large B cell lymphoma, 5 (14%) with MCL, 4 (11%) with follicular lymphoma, 3 (8%) with Hodgkin lymphoma, and 6 (17%) with other types. Disease status at harvest was complete response (CR) in 20 patients (56%) and non-CR in 16 patients (44%) (partial response, 14 patients; stable disease and progressive disease, 1 patient). Prior bone marrow involvement was determined in 16 patients (44%). Four patients (11%) underwent radiotherapy prior to harvest. PBSCs harvest regimens were ESHAP (etoposide, methylprednisolone, cytarabine, cisplatin) in 11 patients (31%); etoposide in 6 (17%); MA (methotrexate, cytarabine) in 5 (14%); DHAP (dexamethasone, cytarabine, cisplatin) in 4 (11%); G-CSF alone in 3 (8%); and other regimen in 7 patient (19%). The median number of regimens and chemotherapy cycles was 2 (range 1–4 cycles) and 9 (range 1–13 cycles), respectively, prior to PBSCs mobilization. Filgrastim was used in 14 patients (39%); lenograstim in 22 (61%). The median number of apheresis procedures was 2 (range 1–3 procedures). Median duration of G-CSF support was 6 days (range 4–10 days). PBSC harvest was performed at a median of 18 days (range 8–22 days) from the start of chemotherapy in 33 patients who underwent chemotherapy followed by G-CSF. The median number of CD34 positive cells collected on the first harvest day was $2.0 \times 10^6/\text{kg}$ (range $0.01\text{--}13.3 \times 10^6$). The median number of CD34 positive cells collected in total was $2.6 \times 10^6/\text{kg}$ (range $0.02\text{--}13.3 \times 10^6$). Number of patients with peripheral monocyte count $>1,000/\mu\text{L}$ on the first harvest day was 27 (75%), and of these, 23 patients underwent successful harvest. Of 36 patients, 27 patients (75%) successfully harvested CD34 positive cells $>2.0 \times 10^6/\text{kg}$. Nine patients (25%) were poor mobilizers. In 33 patients who

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Table 1 Factors associated with mobilizations in 33 patients using chemotherapy

	CD34 positive cells/kg ≥ 2.0 in total (n = 25)	CD34 positive cells/kg < 2.0 in total (n = 8)	P value
Age			
≥ 60	10	3	1
< 60	15	5	
Sex			
Male	10	6	0.118
Female	15	2	
No. of chemotherapy (cycles)			
> 6	17	5	1
≤ 6	8	3	
No. of (regimens)			
> 2	6	4	0.205
≤ 2	19	4	
Previous radiation therapy			
Radiation therapy	2	2	0.241
No radiation therapy	23	6	
G-CSF			
Filgrastim	8	3	1
Lenograstim	17	5	
Bone marrow involvement			
Yes	11	4	1
No	14	4	
Disease status at harvest			
CR	15	4	0.695
Non-CR	10	4	
Stage			
4	10	6	0.118
1,2,3	15	2	
Peripheral WBC count on the first harvest day (μL)			
$\geq 10,000$	12	1	0.108
$< 10,000$	13	5	
Peripheral juvenile cells (blasts, myelocytes, metamyelocytes) count on the first harvest day (%)			
> 10	17	3	0.213
≤ 10	8	6	
Peripheral monocyte count on the first harvest day ($/\mu\text{L}$)			
$> 1,000$	21	3	0.020
$\leq 1,000$	4	5	
Duration of G-CSF support			
≥ 6 days	14	6	0.431
< 6 days	11	2	
Peripheral neutrophil count in nadir ($/\mu\text{L}$)			
< 500	18	7	0.643
≥ 500	7	1	
Platelet count in nadir ($/\mu\text{L}$)			
$< 25,000$	9	5	0.238
$\geq 25,000$	16	3	

G-CSF granulocyte-colony stimulating factor, CR complete response, WBC white blood cell

were using chemotherapy, CD34 positive cell yield was not associated with age ≥ 60 years, sex, prior bone marrow involvement, previous cycles of chemotherapy, previous radiotherapy, lenograstim or filgrastim, neutrophil count and platelet count in nadir as shown in Table 1. Only a peripheral blood monocyte count $>1,000/\mu\text{L}$ on the first harvest day was a predictor of a successful harvest ($P = 0.020$).

Of our study population, 75% of patients were successful in achieving adequate CD34 positive cells. Another report showed that prior fludarabine or alkylating agent therapy was associated with poor PBSC yields [2]. Moreover, a prior study suggested that a higher number of chemotherapy regimens has a negative impact on mobilization efficiency; in addition, the peripheral blood CD34positive cell count was also correlated with PBSC yields [3]. Kim et al. [4] reported that G-CSF injection 3 h prior to apheresis improved the efficacy of stem cells. As described above, various factors were reported to be associated with PBSC harvest. However, in our study, only peripheral blood monocyte count on the first harvest day predicts successful harvest as reported by Yang et al. [5]. Our study has several limitations, one of which is that it was an uncontrolled, retrospective, single-center study. In addition, different initial and harvest chemotherapy regimens were used. It is easy to measure peripheral blood monocyte count rather than peripheral CD34 positive cells counts, suggesting that it will become a reliable and simple

indicator of PBSC harvest. However, further analysis is required in more cases.

Compliances with Ethical Standard

Conflict of interest The author declares that he/she has no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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