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Original article

Autologous stem cell transplantation and stem cell mobilization kinetics in elderly patients with B cell non-Hodgkin lymphoma

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ABSTRACT

As known, the world population is aging and as the life span increases the number of advanced-age lymphomas also shows an upward trend. Autologous hematopoietic stem cell transplantation (HSCT) is the standard treatment modality in chemotherapy-sensitive relapsed or refractory aggressive lymphomas. Increased morbidity and mortality related to both the transplant itself and comorbid diseases can be observed in elderly lymphoma patients. Patients who are 65 years or older and underwent autologous HSCT with B-cell non-Hodgkin lymphoma were retrospectively included in our study. In terms of survival analysis, median follow-up was 34.5 months (8–159) while the overall survival (OS) was 58%. In the univariate analysis of prognostic data in OS, patients who were referred to transplantation with complete response had a statistically significant survival advantage ($p = 0.043$). In terms of the effect of pre-transplant conditioning regimens on survival, BEAM regimen yielded better results, though not statistically significant. Age, number of chemotherapy cycles received before mobilization and radiation therapy had no significant effect on the CD34 (+) cell count in the final product ($p = 0.492$, 0.746 and 0.078 respectively). In conclusion, autologous HSCT is a practicable treatment modality that provides survival advantage in suitable advanced-age patients with a diagnosis of B-cell non-Hodgkin lymphoma.

Contents

1. Introduction

As it is known, the world population is aging and as the life span increases the number of advanced-age lymphomas also

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Table 1
Demographic and clinical characteristics of patients.

Diagnosis	n	Gender (M/F)	Age	ECOG	EF (%)	IPI	NCCN-IPI	Comorbidity (±)
DLBCL	19	14/5	67 (65–72)	1 (0–3)	60 (45–65)	3 (2–5)	4 (3–5)	13/6
MCL	14	11/3	67 (65–71)	1 (0–2)	60 (50–65)	3 (1–5)	4 (2–6)	5/9
FL	2	2/0	66–68	0	60	3	4	1/1
Other								
Plasmoblastic	1	1/0	67	0	60	2	3	1/–
	36	28/8	67 (65–72)	1(0–3)	60 (45–65)	3 (1–5)	4 (2–6)	20/16

DLBCL: Diffuse large B cell lymphoma; MCL: Mantle cell lymphoma; FL: Follicular lymphoma; EF: Ejection fraction; ECOG: Eastern Cooperative Oncology Group; M/F: Male/Female; IPI: International Prognostic Index.

shows an upward trend [1]. Autologous hematopoietic stem cell transplantation (HSCT) is the standard treatment modality in chemotherapy-sensitive relapsed or refractory aggressive lymphomas. Autologous HSCT is used in relapsed or refractory diffuse large B-cell lymphoma (DLBCL) and follicular lymphoma (FL), which are B-cell non-Hodgkin lymphomas (NHL), while there are studies showing the efficiency of autologous HSCT as consolidation in first line treatment in mantle cell lymphoma (MCL) [2–6]. According to the data of Center for International Blood and Marrow Transplant Research (CIBMTR) the number of transplantations in patients older than 70 is rising. In spite of this increase, the efficiency of autologous HSCT in elderly patients is not clear. Increased morbidity and mortality related to both the transplant itself and comorbid diseases can be observed in these patients [7]. Therefore, meticulous functional status and geriatric examination needs to be performed when deciding for autologous HSCT. Also, determining optimal conditioning regimens with prospective studies will lead to decrease in mortality and morbidity. In the light of these data, in our multi-center retrospective analysis we aimed to investigate the transplant results and the rates of transplant-related mortality and morbidity in advanced-age patients who underwent autologous HSCT with the diagnosis of B-cell NHL.

2. Patients and Methods

2.1. Patients

Patients who are 65 years or older and underwent autologous HSCT for relapsed/refractory B-cell NHL or as consolidation in first-line treatment of B-cell NHL were retrospectively included in our study. Comorbidity analysis and stem cell kinetics were evaluated alongside with the demographic and clinical characteristic of the patients. “Sorror” hematopoietic cell transplantation-specific comorbidity index (HCT-CI) was utilized for comorbidity analysis. The risk groups of the patients were determined using IPI and NCCN-IPI scores. Bulky disease was considered as a mass larger than 7.5 cm according to NCCN criteria.

2.2. Statistical Analysis

SPSS version 17.0 was used for statistical analysis in our study. Descriptive statistics were performed for patient characteristics. Categorical variables were compared using chi-squared test. Spearman’s Rho correlation analysis was used for correlation analyses. Cox regression analysis was performed using Kaplan-Meier survival analysis. P value of < 0.05 was considered significant.

3. Results

Thirty-six patients from 6 different centers who underwent autologous HSCT either for relapsed/refractory disease or in first-line treatment as consolidation were included. Twenty-eight patients were male and 8 were female. Of the patients, 19 had a diagnosis of DLBCL, 14 had MCL, 2 had FL and 1 had plasmoblastic lymphoma. Median age was 67 (65–72). Mean ECOG performance score was 1 (0–3). Twenty patients (55.5%) had a comorbid disease (Table 1). When the disease stages at the time of diagnosis were considered, 19 patients had stage 4, 14 patients had stage 3, 2 patients had stage 2, and 1 patient had stage 1 disease. Only 5 patients (13.9%) had bulky masses. When the hepatitis serologies of the patients were examined, 3 patients were found to be positive for HBsAg. One patient had hepatitis reactivation despite antiviral treatment. Mean HCT-CI was 1 (0–3).

Among all patients, 29 patients received R-CHOP chemotherapy protocol as first-line treatment, while 7 received R-CHOP-like and other protocols. Twenty patients achieved complete response (CR) after first-line treatment and developed relapse during follow-up. Partial response (PR) was observed in 4 patients, stable disease (SD) was observed in 6 patients and progression was observed in 6 patients. Patients received a median of 8 (4–14) cycles of chemotherapy before autologous HSCT. Only 5 patients (3 DLBCL and 2 FL) received radiation therapy before transplantation. 6 patients (5 MCL, 1 plasmoblastic lymphoma) underwent autologous HSCT as consolidation in first-line treatment. When the patient response before autologous transplantation was considered, 22 patients were referred to transplantation with CR, 11 patients with PR, 1 with SD and 2 with refractory disease. Median time until autologous transplantation was 14.5 (3–192) months. The most frequent conditioning regimen used was BEAM (BCNU, Etoposide, Cytarabine and Melphalan) protocol (66%). ICE (ifosfamide, carboplatin, and etoposide) regimen was used for conditioning in 6 (16.6%) patients while different regimens were favored according to clinical preference in the remaining 6 patients. HCT-CI was used in all patients before the transplant and 16 patients (44.4%) scored 0, 12 patients (33.3%) scored 1, 6 patients (16.7%) scored 2 and 2 patients (5.6%) scored 3. After the transplantation, 26 patients achieved CR, 3 patients achieved PR and 2 patients achieved stable disease. Post-transplant +100 days mortality was 13.8% with 5 patients (4 DLBCL, 1 MCL).

When the stem cell kinetics were evaluated, chemotherapy plus granulocyte colony stimulating factor (G-CSF) was the most frequent regimen for mobilization (24 patients), followed by G-CSF alone in 6 patients and plerixafor in 6 patients. Median number of apheresis sessions performed was 2, while it could last up to 4 days (Table 2). Age, number of chemotherapy cycles received before mobilization and radiation therapy had no significant effect on the CD34 (+) cell count in the final product ($p = 0.492$, 0.746 and 0.078, respectively).

In terms of survival analysis, median follow-up was 34.5 months (8–159) while the OS was 58% (Fig. 1). Median survival after autologous HSCT was 10 (1–149) months. In the univariate analysis of prognostic data in OS (Table 3), patients who were referred to transplantation with CR had a statistically significant survival advantage ($p = 0.043$) (Fig. 2). In terms of the effect of pre-transplant conditioning regimens on survival, BEAM regimen yielded better results, though not statistically significant (Fig. 3). When the patients were

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