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Brief article

Peripheral Blood Hemopoietic Stem Cell Mobilization Regimens in POEMS Syndrome: A Retrospective Study at 2 Hematologic Italian Centers

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A B S T R A C T

Autologous peripheral blood stem cell transplantation should be considered first-line therapy in young patients with POEMS. The best protocol to collect peripheral blood stem cells remains to be defined, because of the disease rarity and the heterogeneity of published case series. We collected clinical and laboratory data from 25 patients undergoing mobilization, of whom 11 were mobilized using cyclophosphamide (CY) followed by granulocyte colony-stimulating factor (G-CSF) and 14 patients using G-CSF. The incidence of poor mobilization was low and not statistically different between the 2 groups. Both schemes (CY plus G-CSF versus G-CSF alone) were able to harvest a sufficient $CD34^+$ cell dose.

INTRODUCTION

POEMS syndrome is a rare paraneoplastic condition associated with an underlying plasmacellular dyscrasia. POEMS is the acronym referring to the main features of this syndrome: polyradicoloneuropathy, organomegaly, endocrinopathy, monoclonal plasma cell disorder, and skin changes [1-3]. The use of alkylating agents and autologous peripheral blood stem cell transplantation (aPBSCT) seems to be the best strategy in eligible patients [4-8]. At present, aPBSCT should be considered first-line therapy in young patients with POEMS syndrome, eligible for high-dose melphalan (HD-Mel), in the absence of organ dysfunction. The optimal protocol for hematopoietic stem cell (HSC) mobilization in patients with POEMS remains to be defined, due to small numbers of patients and heterogeneity of published case series. However, there is evidence that cyclophosphamide (CY) plus granulocyte colony-stimulating factor (G-CSF) mobilizes more $CD34^+$ cells and reduces the incidence of engraftment syndrome in patients with POEMS, although it may potentially increase the risk of the procedure, without a significant reduction of tumor mass [9,10].

METHODS

In this undefined scenario, Fondazione Policlinico Universitario Agostino Gemelli IRCCS (FPG) and Humanitas Research Hospital (HRH) retrospectively collected over the years patients with POEMS syndrome mobilized with different regimens and compared the outcome of these regimens. We are now reporting the results of this study, aimed at identifying, if possible, the best $CD34^+$ cell mobilization strategy.

We collected clinical and laboratory data of patients with POEMS syndrome undergoing HSC mobilization for aPBSCT from 2003 to 2018 at FPG and HRH. The minimum dose for transplant was defined as 2×10^6/kg $CD34^+$ cells.

We compared 2 HSC mobilization regimens: CY 4 g/m^2 followed by G-CSF 5 μg/kg, or G-CSF 10 μg/kg/d alone for 5 consecutive days. The COBE Spectra continuous flow cell separator (Terumo BCT, Shinagawa, Tokyo) was used for leukocytapheresis, and citrate dextrose solution was used as anticoagulant. Patients were defined as poor mobilizers if they were not able to mobilize at least 20 $CD34^+$ cells/μL or obtain a minimum threshold of 2×10^6/kg $CD34^+$ cells within a single mobilization. The conditioning regimen before aPBSCT consisted of melphalan 200 mg/m^2 for all patients.

Data, collected by medical records and laboratory tests, were organized to perform a statistical analysis using GraphPad Prism (GraphPad Software, San Diego, CA). Mann-Whitney *U* test was used to analyze continuous factors, and chi-square test was chosen for the analysis of the categorical factors. The results of hematopoietic recovery were analyzed according to the Kaplan-Meier method. Statistical significance was defined as $P < .05$.

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Table 1
Peripheral Blood Stem Cell Collection Characteristics According to Mobilization Schedule

Characteristic	Total (n = 25)	Cyclophosphamide plus G-CSF (n = 11)	G-CSF (n = 14)	*P* Value
Age	54 (39-67)	55 (39-62)	54 (41-67)	.9
Precollection peripheral CD34$^+$, μL	40 (12-308)	57 (12-308)	33 (14-75)	.035
Precollection peripheral WBCs, $\times 10^9$/L	29.4 (2.5-87)	8.1 (2.5-31.9)	40 (20.2-87)	.0002
Processed TBVs	2.85 (0.9-3.5)	2.3 (0.9-3)	3 (2.4-3.5)	.0013
CD34$^+$collected cell dose, $\times 10^6$/kg	3.85 (0.8-15)	3.85 (1.6-15)	3.85 (0.8-7.5)	.41
Second procedure, n	11	4	7	.68
Poor mobilizers, n	3	1	2	.69
CD34$^+$ cell dose infused, $\times 10^6$/kg	4.7 (2.5-8.4)	4.4 (2.986-7.5)	5 (2.5-8.4)	.57
Time to engraftment PMNs 0.5 $\times$ 10^9/L	14.5 (10-48)	14 (10-31)	19 (12-48)	.12
Time to engraftment PLTs 25 $\times$ 10^9/L	14 (10-67)	13 (10-35)	17 (11-67)	.14

Values are presented as median (range) unless otherwise indicated.
PLTs indicates platelets.

RESULTS

Our data set consisted of 25 patients, of whom 11 were mobilized using regimen A (CY 4 g/m^2 followed by G-CSF 5 μg/kg), and 14 patients were mobilized with regimen B (G-CSF 10 μg/kg for 5 days). All patients received antibiotic prophylaxis with trimethoprim/sulfamethoxazole; we registered 2 episodes of fever of unknown origin in regimen A, without further complications. All patients were mobilized: median preapheresis CD34$^+$ cell count was 40 (12 to 308) with a median WBC count of 29.4 $\times$ 10^9/L (range, 2.56 to 87). Median whole-blood processed volume was 2.85 total blood volumes (TBVs) (0.9 to 3.5). Median CD34$^+$ cell/kg body weight collected per patient after first cell collection procedure was 3.85 $\times$ 10^6/kg (0.8 to 15). Eleven of 25 (44%) patients repeated a stem cell apheresis on the following day: median preapheresis CD34$^+$ cell count before the second procedure was 31 (11 to 65) with a median WBC count of 31.4 $\times$ 10^9/L (range, 9 to 82). Median whole-blood processed volume was 3 TBVs (2-3.2). Median CD34$^+$ cell/kg body weight collected per patient during the second cell collection procedure was 2.6 $\times$ 10^6/kg (0.4 to 6.4). Because of a low CD34$^+$ cell count ($<$20/μL), 3 patients were treated with plerixafor, achieving a median preapheresis CD34$^+$ cell count of 28/μL, and collected a median CD34$^+$ cell/kg of 4.5 $\times$ 10^6/kg body weight. All patients underwent aPBSCT after the HD-Mel conditioning regimen and received an infusion of a median of 4.7 $\times$ 10^6 (range, 2.5 to 8.4) CD34$^+$ cell/kg body weight. All patients achieved a successful engraftment: median time to 500 polymorphonuclear leukocytes (PMNs)/μL was 14 days (range, 10 to 48); median time to 1000 PMNs/μL was 15 days (range, 10 to 54); median time to 25 $\times$ 10^9 platelets/L was 14 days (range, 10 to 67); and median time to 50 $\times$ 10^9 platelets/L was 19.5 days (range, 13 to 84). After aPBSCT hospitalization, 13 patients (52%) experienced fever, and pneumonia was diagnosed in 6 patients, which was resolved successfully with broad-spectrum antibiotics.

To compare mobilization schedules, we performed a comparison analysis between 11 patients receiving chemotherapy as a mobilizing regimen versus 14 patients receiving only G-CSF. Data analysis according to mobilization schedule are reported in Table 1.

DISCUSSION

Analyzing mobilization efficacy, chemomobilized patients achieved a higher preapheresis CD34$^+$ cell count (57 versus 33 cells/μL, $P < .05$). This result allowed a significantly shorter procedure (2.3 versus 3 TBVs, $P < 0.001$). However, patients receiving G-CSF alone had a significantly higher WBC count than chemomobilized patients (40 $\times$ 10^9/L versus 8.1 $\times$ 10^9/L, $P < .05$). The need for the use of plerixafor was low (3 of 25 patients, 12%) and not statistically different between the 2 mobilization schedules. No statistically significant differences were seen between the 2 groups in terms of engraftment. The analysis on immune recovery showed a good reconstitution of lymphocytes counts and immunoglobulin levels within the first 30 days after aPBSCT, with no difference between our 2 groups of patients. These data are similar to previously published immunologic recovery in patients with lymphoproliferative diseases [11,12].

In conclusion, these results suggest that both approaches for mobilization of peripheral blood progenitors (CY plus G-CSF versus G-CSF alone) were able to harvest a sufficient CD34$^+$ cell dose and allow good and rapid engraftment. Despite the small number of patients (n = 25), this remains one of the largest published series. In the future, purging before harvest with lenalidomide, shown to produce complete responses documented by vascular endothelial growth factor values without compromising the harvest, could be compared with first-line treatments.

DECLARATION OF COMPETING INTEREST

There are no conflicts of interest to report.

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