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Outcome of Allogeneic and Autologous Hematopoietic Cell Transplantation for High-Risk Peripheral T Cell Lymphomas: A Retrospective Analysis From a Chinese Center

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A B S T R A C T

Peripheral T cell lymphomas (PTCLs) often carry poor outcomes with conventional chemotherapy, and hematopoietic cell transplantation (HCT) can benefit patients with PTCL. We conducted a retrospective review of 67 patients with PTCL who underwent autologous HCT (autoHCT, n = 43; median age, 40 years) or allogeneic HCT (alloHCT, n = 24; median age, 36.5 years) from 2004 to 2016. With a median follow-up of 27 months, 5-year progression-free survival (PFS) and overall survival (OS) of autoHCT patients were 49% and 57%, respectively. Among alloHCT recipients, the 5-year PFS and OS were 54% and 55%, respectively. When considering incidence of disease relapse or progression (CIR) and nonrelapse mortality (NRM), the 5-year CIR and 1-year NRM of alloHCT recipients were 38% and 18%, respectively, and 58% and 7% for autoHCT patients, respectively. There were no differences between autoHCT and alloHCT in 5-year PFS ($P = .499$), OS ($P = .566$), CIR ($P = .555$), and NRM ($P = .202$). When specifically examining recipients in primary refractory disease, 3-year PFS rates of autoHCT and alloHCT were 20% and 49% ($P = .054$); 3-year OS rates were 20% and 53% ($P = .042$), respectively. Based on these results, we favor proceeding to alloHCT in patients with PTCL in primary refractory disease.

INTRODUCTION

Peripheral T cell lymphomas (PTCLs) are a heterogeneous group of non-Hodgkin lymphomas, the occurrence of which in western countries is relatively low, but it is relatively high in East Asia (China 32.5 %, Korea 22 %, and Japan 24.9 %) and Southeast Asia (Thailand 25 %) [1]. The most common types of PTCLs are PTCL-not specified, angioimmunoblastic T cell lymphoma, and anaplastic large cell lymphoma (ALCL). Compared with the aggressive B cell lymphomas, PTCL has a poor outcome with standard treatments, and the International T cell Lymphoma Project highlights that the 5-year disease-free survival was below 30% [2].

Given the poor outcomes with conventional chemotherapy, hematopoietic cell transplantation (HCT) has been offered to patients with PTCL. Recent retrospective studies have reported that autologous HCT (autoHCT) as consolidation can offer a durable survival benefit in high-risk patients with first complete or partial response, and allogeneic HCT (alloHCT) could result in long-term disease control for relapsed and refractory patients [3]. However, questions about the optimal timing for stem cell transplantation and relative efficacy of autoHCT versus alloHCT remain a matter of opinion. We conducted a retrospective review and report the clinical outcomes of 67 patients with high-risk PTCLs who underwent HCT in a single center during the past 12 years.

MATERIALS AND METHODS

Patients

We retrospectively reviewed the records of patients with PTCL who underwent HCT from July 2004 to December 2016 in our center. Eligibility

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criteria were the following: (1) histologically proven diagnosis of PTCL according to the World Health Organization classification; (2) International Prognostic Index score of ≥3; (3) Eastern Cooperative Oncology Group performance status of <2; (4) preserved adequate cardiac, hepatic, and renal function before transplantation; (5) and the absence of second transplantations.

Response Assessment and Toxicity Criteria

The response to therapy was evaluated according to Cheson criteria after the induction phase, before transplantation, 1 month after transplantation, and then every 3 months for the first year and every 6 months thereafter. Toxicity assessment was performed according to National Cancer Institute Criteria for Adverse Events, version 3.0.

Statistics

The primary endpoints studied were overall survival (OS) and progression-free survival (PFS). *OS* was defined as the time from transplantation to death from any cause and *PFS* was defined as the time from transplantation to relapse or progressive disease or death from any cause. Secondary endpoints were incidence of disease relapse or progression (CIR) and nonrelapse mortality (NRM). *NRM* was defined as death as a result of any cause without evidence of lymphoma relapse or progression. The probabilities of OS and PFS were calculated by the Kaplan-Meier method and compared by a log-rank test. Estimates of lymphoma relapse or progression and NRM were calculated using cumulative incidence curves.

RESULTS

Patient Characteristics

From July 2004 to December 2016, 67 patients met the inclusion criteria. Of these, 43 patients underwent autoHCT and the other 24 patients received alloHCT. PTCL-not specified was the underlying disease in 37 patients (55.2%), anaplastic lymphoma kinase–negative ALCL in 19 (28.4%), natural killer/T in 10 (14.9%), and angioimmunoblastic T cell lymphoma in 1 (1.5%). Patient characteristics are listed in Table 1. Most patients in both groups had B symptoms, disease stage of IV, and extranodal disease at time of diagnosis. There were no differences in median age, sex, disease stage, and lines of therapy before transplantation by HCT type. However, autoHCT patients had more ALCL histology and alloHCT recipients had longer time from diagnosis to transplantation.

Table 1
Patient Characteristics

Characteristic	Auto-HCT		Allo-HCT		*P*
	No.	%	No.	%	
No. of patients	43		24		
Sex					.927
Male	30	69.8	17	70.8	
Female	13	30.2	7	29.2	
Age at transplantation, yr					.850
Median (range)	40 (7-63)		36.5 (16-52)		
Histology					.007
PTCL-NOS	20	46.5	17	70.8	
ALK-negative ALCL	18	41.9	1	4.2	
AITL	0	0	1	4.2	
NK/T	5	11.6	5	20.8	
B symptoms at diagnosis	24	55.8	13	54.2	.897
BM involvement at diagnosis	11	25.6	10	41.7	.174
Extranodal involvement at diagnosis	29	67.4	19	79.2	.307
Disease stage at diagnosis					.053
III	17	39.5	4	16.7	
IV	26	60.5	20	83.3	
No. of lines of therapy before transplantation					.091
≤2	32	74.4	13	54.2	
>2	11	25.6	11	45.8	
Time from diagnosis to transplantation, mo					.013
Median (range)	6 (2-21)		10 (2-89)		

PTCL-NOS indicates PTCL-not specified; ALK-negative ALCL, anaplastic lymphoma kinase-negative anaplastic large cell lymphoma; AITL, angioimmunoblastic T cell lymphoma; NK/T, natural killer/T cell; BM, bone marrow.

Treatment Characteristics

Most patients received 4 courses of cyclophosphamide, daunorubicin, vincristine, and prednisone (CHOP) with or without etoposide as initial induction therapy. If complete remission (CR) were not achieved, 2 additional cycles CHOP regiment or some second-line regiments were allowed, such as etoposide, methylprednisolone, cytarabine, and cisplatin or dexamethasone, cytarabine, and cisplatin.

Patients underwent autoHCT mobilized by cytarabine 2 g/m^2 every 12 hours on day 1 and 2, mitoxantrone 10 mg/m^2 on days 2 and 3, Recombinant human granulocyte colony-

Table 2
Transplantation-Related Characteristics

Characteristic	AutoHCT		AlloHCT		*P*
	No.	%	No.	%	
Disease status at transplantation					<.01
CR1	20	46.5	0	0	
CR2	6	13.9	2	8.3	
PR	7	16.3	6	25.0	
NR	10	23.3	16	66.7	
Conditioning regimen (auto)			NA		
BEAM	38	88.4			
Other*	5	11.6			
Conditioning regimen (allo)	NA				
TBI/Cy			6	25.0	
Bu/Cy			18	75.0	
Type of donor	NA				
HLA-identical sibling			3	12.5	
Matched unrelated			5	20.8	
Mismatched related			16	66.7	
Donor-recipient sex match	NA				
Male to male			9	37.5	
Male to female			5	20.8	
Female to male			7	29.2	
Female to female			3	12.5	
Tissue for graft	NA				
BM			1	4.2	
PB			11	45.8	
BM+PB			4	16.7	
BM+PB+CB			8	33.3	
GVHD prophylaxis	NA				
CSA+MTX			5	20.8	
ATG+CSA+MMF+MTX			19	79.2	
GVHD	NA				
aGVHD			9	37.5	
cGVHD			4	16.7	
Responses to transplantation					.695
CR	28	65.1	14	58.3	
PR	9	20.9	7	29.2	
NR	4	9.3	1	4.2	
Death	2	4.7	2	8.3	
Status at last contact					.563
Dead	15	34.9	10	41.7	
AWD	5	11.6	1	4.2	
NED	23	53.5	13	54.1	
Time from transplantation to relapse, months					.568
Median	6		8		
Range	2-59		1-27		

PR indicates partial remission; NR, no remission; NA, not available; BEAM, semustine/carmustine, etoposide, cytarabine, melphalan; TBI/Cy, total body irradiation, cyclophosphamide; Bu/Cy, busulfan, cyclophosphamide; BM, bone marrow; PB, peripheral blood; CB, cord blood; GVHD, graft-versus-host disease; CSA, cyclosporine; MTX, methotrexate; ATG, antithymocyte globulin; MMF, mycophenolate mofetil; aGVHD, acute GHVD; cGVHD, chronic GVHD; AWD, alive with disease; NED, no evidence of disease.
*Other conditioning regimens include semustine/carmustine, etoposide, cytarabine and cyclophosphamide (n = 4) and TBI/Cy (n = 1).