The outcomes of allogeneic stem cell transplantation in patients with mixed phenotype acute leukemia (MPAL) are comparable to those in AML and ALL: Results of matched-pair analysis

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Introduction

Mixed phenotype acute leukemia (MPAL) is a rare subtype of acute leukemia that accounts for 2-5% of all acute leukemia cases. It has been reported that patients with MPAL tend to have worse prognosis compared with those with acute myeloid leukemia (AML) or acute lymphoblastic leukemia (ALL). However, the efficacy and safety of allogeneic stem cell transplantation (allo-SCT) for adult MPAL patients has yet to be elucidated. The aim of this retrospective study was to assess the outcome of allo-SCT for adult MPAL and compared with those for AML/ALL by matched pair analysis.

Patients & Methods

Study population

This study included all consecutive adult acute leukemia patients aged over 15, who underwent allo-HSCT for the first time between January 2001 and December 2010 at the seven institutions participating in the Kanto Study Group for Cell Therapy (KSGCT). Their clinical data were collected from the KSGCT database. The clinical features and transplant outcomes of MPAL patients were compared with those of adult patients with AML, ALL, and Philadelphia chromosome-positive acute leukemia (Ph-AL). Control cohorts were extracted from the same database by using an optimal matching method.

Table 1

Diagnostic criteria

Myeloid	
Myeloperoxidase	
OR	
Monocytic differentiation (at least two of the following: NSE, CD11c, CD14, CD64, lysozome	
T lineage	
Cytoplasmic or surface CD3	
B lineage	
Strong CD19 AND at least one of the following with strong expression: CD79a, cytoplasmic CD22, or CD10	
OR	
Weak CD19 AND at least two of the following with strong expression: CD79a, cytoplasmic CD22, or CD10	

Definitions

Diagnostic criteria of MPAL according to WHO classification was shown in Table 1.

Statistical Analysis

Overall survival (OS) was defined as the interval from the date of transplantation to the date of death by all causes. Relapse-free survival (RFS) was defined as the interval from the date of transplantation to the date of relapse or the date of death in CR whichever came first. Non-relapse mortality (NRM) was defined as any death in continuous complete remission (CR). The Fisher's exact test was used for comparison of binary variables. OS and RFS were estimated by the Kaplan-Meier method, and compared using the log-rank test. Cumulative incidences (CI) of relapse and NRM were compared using the stratified Gray test. All calculations were performed using the EZR software package (http://www.jichi.ac.jp/saitama-sct/SaitamaHP.files/statmed.html), and $p < 0.05$ was considered as statistically significant.

Result 1. Patient characteristics

Patient characteristics and transplant procedures (Table 1, 2)

Of the 1074 acute leukemia patients who met the inclusion criteria, 18 MPAL patients (1.7%) were identified. Patient characteristics and transplant procedures of 18 MPAL patients were shown in Table 1A and 1B. As the initial induction chemotherapy, 10 patients received ALL-type chemotherapy, and eight patients received AML-type chemotherapy. All seven Ph-MPAL patients received imatinib during pre-transplant period, but not as post-transplant maintenance therapy.

Table 2A

Baseline characteristics

Background (n = 18)	
Median age (range)	40 (16 - 61)
M / F, n	9 / 9
CR / non-CR, n	13 / 5
Immunophenotype, n (%)	
B + M	12 (67)
T + M	5 (28)
B + T + M	1 (6)
Cytogenetics, n (%)	
Ph-positive	7 (39)
Normal	6 (33)
Others	5 (28)

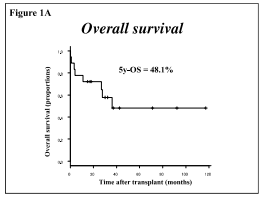
Table 2B

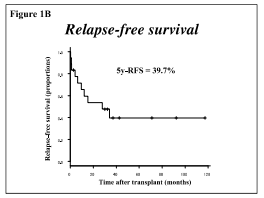
Transplant procedures

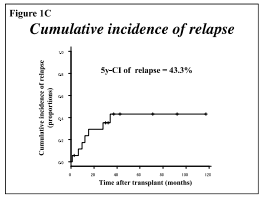
Donor type, n (%)	
Related	4 (22)
Unrelated	13 (72)
Cord blood	1 (6)
Conditioning regimen, n (%)	
MAC	16 (89)
TBI-containing	16 (89)
Time of transplant, n (%)	
2001 - 2005	3 (17)
2006 - 2010	15 (83)

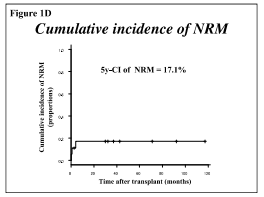
Result 2. Transplant outcomes in MPAL patients

The 5-year OS and RFS rates and 5-year cumulative incidence of relapse and NRM were shown in Figure 1A, 1B, 1C, and 1D.



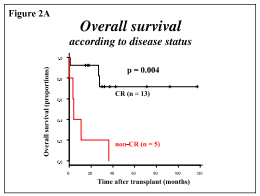


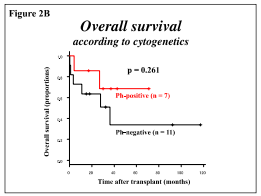


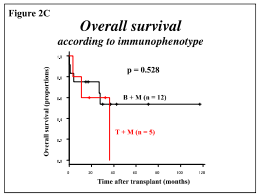


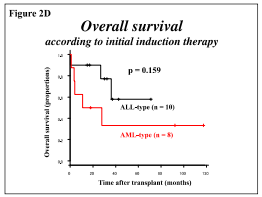
Factors affecting on OS in MPAL patients.

Being in remission at the time of transplant was the only factor significantly associated with better OS (5-year OS: 71.8% vs. 0%, p = 0.001) **(Figure 2A)**. No significant difference was seen in OS when stratifying patients according to immunophenotype, cytogenetic abnormalities (with or without Ph), and initial induction therapy (AML-type or ALL-type) **(Figure 2B, 2C, 2D)**.









Result 3. Matched-pair analysis

Extraction of control cohorts

We selected control cohorts at the rate of one to five using an optimal matching method with the seven matching factors shown in Table 2. Ninety AML and ALL patients and 35 Ph-AL patients were extracted.

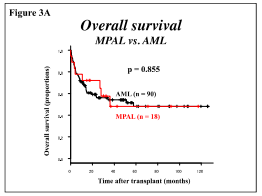
Table 3

Matching factors

1. Age (<50 or 50-<=)
2. Sex
3. Disease status (CR or non-CR)
4. Intensity of conditioning (according to EBMT criteria)
5. HLA disparity (match or mismatch)
6. Donor type (related or not)
7. Time of transplant (2001 - 2005 or 2006 - 2010)

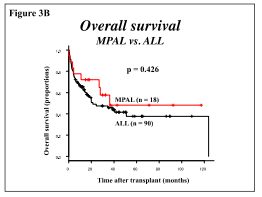
MPAL vs. AML

The 5-year OS rate of MPAL patients was similar to those of AML patients (48.1% vs. 48.1%; p = 0.855). No significant difference was observed in RFS and cumulative incidence of relapse and NRM.



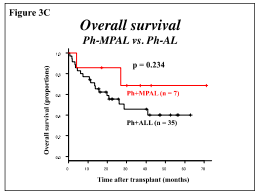
MPAL vs. ALL

The 5-year OS rate of MPAL patients was similar to those of ALL patients (48.1% vs. 38.7%; p = 0.426). No significant difference was observed in RFS and cumulative incidence of relapse and NRM.



Ph-MPAL vs. Ph-AL

The 5-year OS rate of Ph-MPAL patients was similar to those of Ph-AL patients (68.6% vs. 39.9%; p = 0.234). No significant difference was observed in RFS and cumulative incidence of relapse and NRM.



Conclusion

Although the number of patients with MPAL analyzed was small, our matched pair analysis suggested that the transplant outcomes of adult MPAL patients were comparable to those of both AML and ALL patients. Our data strongly recommended to perform transplant for MPAL early in the disease course, preferably in remission, as the transplant outcome of patients not in remission was dismal. Innovative transplant approaches are clearly warranted to improve the transplant outcome of MPAL patients who are not in remission.

Conflict-of-Interest

This work had no specific funding and the authors declare no competing financial interests.