пациентов старше 45 лет результаты алло-ТГСК в ПР1 противоречивые, за счет высокой трансплантационной летальности.

Ключевые слова

Острый В-лимфобластный лейкоз, Ph-позитивный, алло-ТГСК.

AL-07

Modern approaches to predicting post-transplant relapse of acute myeloid leukemia in children

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Introduction

Relapse of acute myeloid leukemia (AML) after allo-HSCT remains one of the main causes of treatment failure. Classical approaches for predicting the risk of AML recurrence after allo-HSCT are based on detection of minimal residual disease (MRD) by flow cytometry and molecular biology studies of recurrent aberrations. Recent studies of gene characteristic of leukemic stem cells (LSCs) defined at the onset of the disease have shown independent prognostic value for children with AML. Data on the pre-transplant level of LSC expression can serve as an additional tool in assessing the risk of post-transplant AML relapse. The aim of our study was to evaluate the influence of MRD status on the results of allogeneic HSCT (allo-HSCT) in children with AML, being determined both by classical methods and according to the genes characteristic of LSCs.

Materials and methods

To assess the MRD by classical approaches, we analyzed data of 95 children with AML in the 1st and 2nd remission. Allo-HSCT was performed over the period of 2008 to 2021. The median age at the time of allo-HSCT was 8 years (5 months to 19 years). Negative MRD status was documented in 67 (70.6%) patients, 28 (29.4%) children had a positive MRD status according to molecular genetic studies and/or immunophenotyping results. Myeloablative conditioning (MAC) was given to 58 (61%) patients, reduced-intensity conditioning (RIC) was performed in 37 (39%) patients. Allo-HSCT from full-matched related donors was performed in 13 (15%) patients; from unrelated donors, in 48 cases (50%); from haploidentical donors, in 34 (35%) patients. All patients received GVHD prophylaxis including post-transplant cyclophosphamide (PtCy) in 59 cases (68%). For pre-transplant evaluation of the LSC gene expression, RT-PCR was performed for the bone marrow samples of 50 patients. At the time of allo-HSCT, 37 (74%) children with AML were in 1st or 2nd remission, whereas 13 (26%) exhibited active disease. The median age in this cohort was 6 (1-18) years. Among the patients in 1st or 2nd AML remissions, 3 children (8%) received allo-HSCT from a full-matched sibling donor; 15 (41%), from an unrelated donor; 19 (51%), from a haploidentical donor. GVHD prophylaxis based on PtCy was received by 29 patients (78%). The DNMT3B, GPR56, CD34, SOCS2, SPINK2, IL2RA, FAM30A, and ABL genes were studied by real-time PCR, followed by calculation of the pLSC6 score using the following formula: (DNMT-3b*0.189)+(GPR56*0.054)+(CD34*0.0171)+(SOCS2*0.141) +(SPINK2*0.109)+(FAM30A*0.0516).

Results

At a 5-year median follow-up in MRD+ patients detected by standard methods, the OS is 67.9% *vs* 73.1% in MRD(-) patients (p=0.83). Relapse-free survival (RFS) was 53.6% *vs* 80.6%, respectively (p=0.01). When assessing expression levels of the genes characteristic of LSC, 18/37 patients (49%) were assigned the pLSC6 level above the median. Only 6/18 patients in 1st or 2nd remission with high pLSC6 were MRD-positive. The linear regression analysis included the patients with pre-transplant response, as well as patients with active disease. It did not show any association between blast counts/MRD and pLSC6 values (OR 1.002; 95% CI: 0.979, 1.025). The 1-year RFS in the CR patients was not significantly different between low-pLSC6 (78.9%) and high-pLSC6 (66.7%) cases (p=0.62). The early relapse rate in CR patients was significantly higher in high-pLSC6 subgroup compared to low-pLSC6 (22% and 0%, accordingly; p=0.03).

Conclusions

Minimal residual disease status before allo-HSCT does not exert a statistically significant effect upon OS. However, MRD-positivity negatively affects RFS values. The pre-transplant level of genes characteristic of LSC showed prognostic significance independent of classical methods for assessing MRD, with respect to early post-transplant AML relapse in children.

Keywords

Acute myeloid leukemia, allogeneic hematopoietic stem cell transplantation, minimal residual disease, leukemic stem cells.