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Chimaerism analysis after allogeneic haematopoietic stem cell transplantation in Lithuanian children

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The aim of this study was to analyse the chimaerism kinetics in children after allogeneic HSCT performed in Vilnius University Children's Hospital. The review focused on the relationship of chimaerism kinetics and clinical course. In addition, the impact of different pre-transplant variables on the chimeric state was proven.

Patients and methods. The patients' cohort consisted of 19 children with malignant and non-malignant haematological disorders. Stem cells were procured from HLA-identical siblings and HLA-matched unrelated donors. Chimeric state was assessed by means of multiplex-PCR using STR polymorphisms. The analysed DNA was extracted from whole blood leukocytes.

Results. Complete DC developed in 47.4% (9/19), MC did in 52.6% (10/19) of patients. The children with non-malignant disorders showed stable and increasing MC patterns meanwhile the leukaemic patients revealed exclusively increasing MC. Development of MC was consistent with non-malignant disorder ($p = 0.033$) and non-myeloablative conditioning ($p = 0.033$). In 2 of 5 non-malignant patients MC was followed by graft rejection whereas in patients with haematological malignancies MC was found to be strongly associated with leukaemic relapse ($p = 0.002$). Both events were the principal factors that limited OS in patients with MC to 50.0%. On the contrary, patients with DC succumbed mostly to the transplant related mortality ($p = 0.049$) resulting in similar OS of 55.6%.

Conclusions. Chimeric state had no significant impact either on the EFS ($p = 0.435$) or on the OS ($p = 0.601$). The results confirmed the reports of other European centres that studied chimaerism kinetics and are consistent with the current transplant practice in Europe.

Key words: Chimaerism, allogeneic haematopoietic stem cell transplantation, short tandem repeats

INTRODUCTION

Allogeneic HSCT is a relatively novel treatment modality offered to the patients with otherwise untreatable haematological disorders like leukaemia, acquired and congenital BM failure and others. The first successful HSCT was performed in 1968 to a patient with severe combined immune deficiency who received bone marrow from an HLA-identical sibling (1). Since that time the number of transplants has been growing up substantially and nowadays has reached approximately 9000 allogeneic transplants per year in Europe (2).

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The first allogeneic HSCT in Lithuania was performed in 1999 to an adult patient. Since February 2002, the treatment has become available for paediatric patients as well. All the Lithuanian children have been transplanted in Vilnius University Children's Hospital, which is the first and the largest Paediatric Transplant Centre in the Baltic States. Both related and unrelated transplants are available (Fig. 1) resulting in internationally reported survival rates (3–5).

Transplant results are strongly dependent on the engraftment of the infused stem cells that is assessed by chimaerism analysis (6). The term chimaerism derives from Greek mythology where Chimaera was a creature with the head of a lion, the body of a goat and the tail of a snake (Fig. 2). In haematology chimaerism reflects the ratio of donor and recipient cells after haematopoietic transplantation. Chimaerism analysis is crucial for the evaluation of the engraftment quality. Monitoring of the chimeric state enables assessment of the risk of transplant rejection,

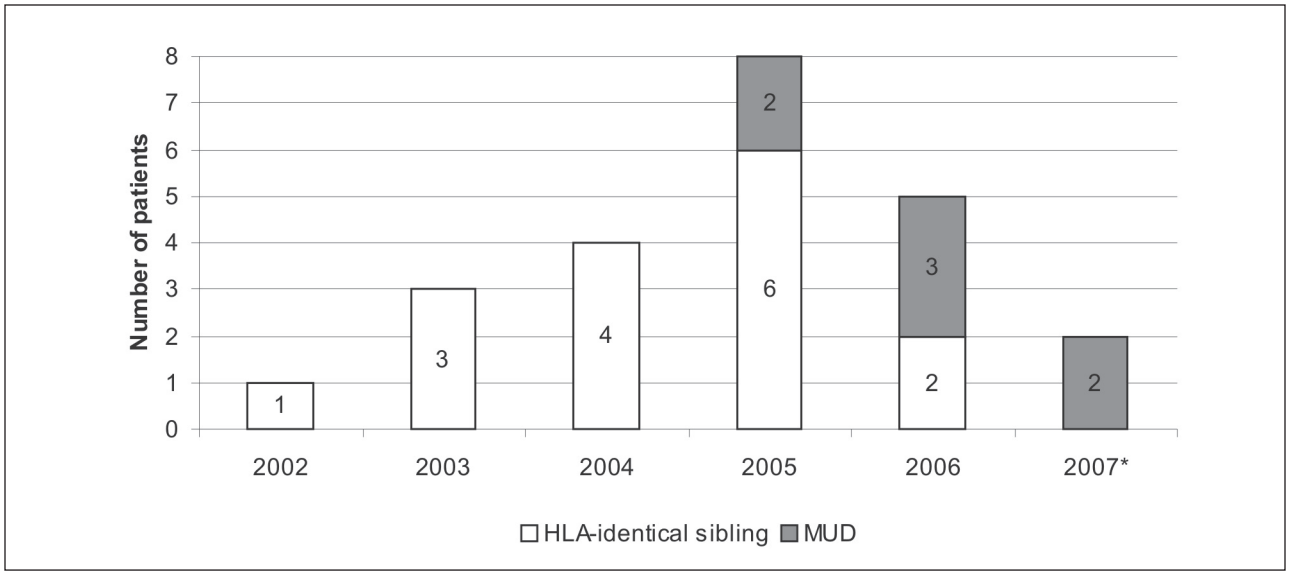

Fig. 1. Annual number of allogeneic transplants performed in Vilnius University Children's Hospital (*data until 01.05.2007)

Fig. 2. Chimaera in Greek mythology

severity of GvHD, probability of leukaemic relapse, haematological and immune reconstitution, and metabolic graft function (7). GvHD, probability of leukaemic relapse, haematological and immune reconstitution, and metabolic graft function (7).

Several techniques have been elaborated for chimaerism analysis. PCR-based procedures using STR polymorphism, especially commercially available multiplex assays, are frequently used (8). STR are highly polymorphic DNA sequences in the human genome that is used for human identity testing and to monitor bone marrow engraftment after allogeneic transplantation. Engraftment analysis requires at least one or more informative STR loci that could reliably distinguish recipient from donor. The sensitivity of the fluorescence-based STR-PCR detection was reported to be 1–5% (9–11). For monitoring of the engraftment, a quantitative, non-isotopic method using a PCR-STR marker has been set up in the Laboratory of Biomedical Research Centre (Vilnius, Lithuania) from July of 2005 (12).

The aim of the present study was to evaluate the impact of the chimaerism kinetics on the transplant results in the Lithuanian paediatric patients.

PATIENTS AND METHODS

Study design and chimaerism definition

Paediatric patients were retrospectively analysed after allogeneic HSCT. Medical records and chimaerism assays were reviewed. Patients included in the study were divided in two groups based on their chimeric state: those with DC and those with MC. MC was defined as 1% or more recipient cells in two consecutive analyses; 100% of donor-derived cells were defined as DC.

Chimaerism kinetics was monitored in whole blood leukocytes. Thereafter cell kinetics pattern was compared parallel to the clinical course. Then, the pre-transplant variables (underlying disorder, conditioning, donor type, stem cell source and dose) were proven for their impact on the chimeric state. Finally, the main outcome parameters (EFS, RFS and OS) were compared in both patients' groups.

The data evaluation was completed in May 2007.

The study was approved by the Lithuanian Bioethics Committee.

Patients

Between February 2002 and May 2007, overall 21 children underwent an allogeneic HSCT in Vilnius University Children's Hospital. Two patients were excluded from the review: one because of early toxic death on day +16 after HSCT before the engraftment occurred, the second one because of insufficient follow-up of less than one week. Thus, in total, 19 patients were included in the study.

Main characteristics of the patients are summarized in Table 1. The majority of the children (73.7%, 14/19) were transplanted

because of different type of leukaemia (Fig. 3). ALL and AML were predominant underlying malignancies (31.6% and 26.3%, respectively). Five of nineteen patients (26.3%) had non-malignant disorders. At the time of HSCT most of the patients were of pre-school age or adolescents (Fig. 4) who corresponded to the leukemia peak-incidence (13). Fifteen of nineteen patients (78.9%) underwent HSCT from their HLA-genotypic identical siblings meanwhile an unrelated transplant from HLA-matched unrelated donor was performed only on four of them (21.1%). BM was the principal source of stem cells. The graft was infused after the disease-specific conditioning (Table 1). Standard GvHD prophylaxis with cyclosporin and methotrexate was applied (14) with addition of antitymocytic immunoglobulin in unrelated transplants.

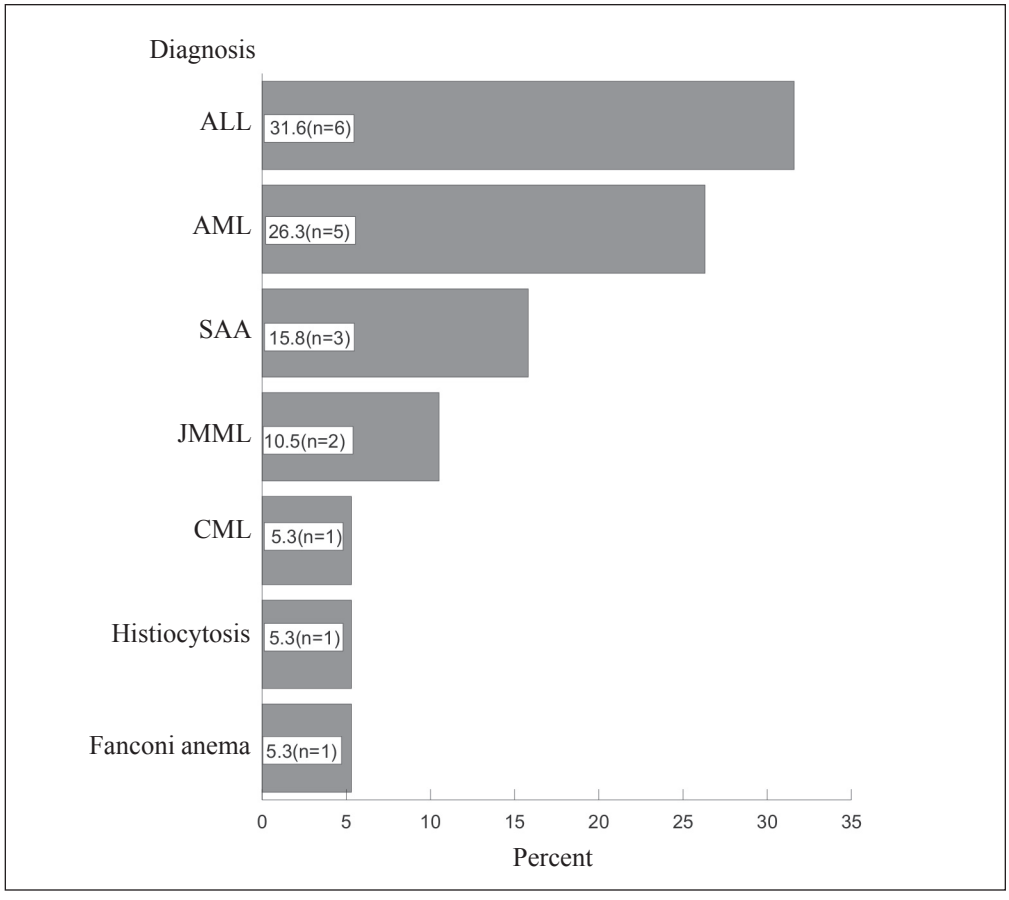

Fig. 3. Distribution of diagnoses

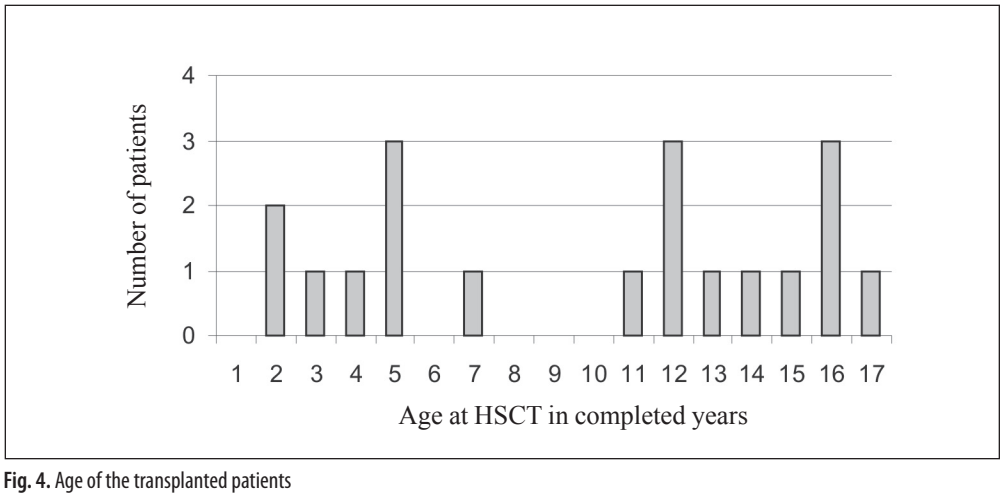

Fig. 4. Age of the transplanted patients

Table 1. **Clinical characteristics and outcome of the patients (n = 19)**

UPN	Diagnosis	Disease stage before HSCT	Donor	Stem cell source	Conditioning	Chimaerism	Grade of acute GvHD	Grade of chronic GvHD	Outcome	OS (days after HSCT)
3	SAA	n.a.	HLA-sib	BM	Cyc+ATG*	MC	II	local	CR	1833
5	AML (M7)	1CR	HLA-sib	PB	Bu/Cyc	MC	0	local	Relapse	981 (†)
7	AML (M2)	1CR	HLA-sib	PB	Bu/Cyc	MC	0	0	Relapse	273 (†)
11	T-ALL	2CR	HLA-sib	PB	Bu/Cyc/Eto	MC	0	0	Relapse	270 (†)
13	AML (M0)	1CR	HLA-sib	BM	Bu/Cyc	DC	0	0	CR	1154
16	SAA	n.a.	HLA-sib	BM	Cyc+ATG*	MC	0	0	Transplant rejection	1049
17	T-ALL	1CR	HLA-sib	PB	Bu/Cyc/Eto	DC	II	0	CR	1028
19	Pre-B-ALL	2CR	HLA-sib	PB	Bu/Cyc/Eto	DC	III	n.e.	TRM	85 (†)
24	CML	CF	HLA-sib	BM	Bu/Cyc	DC	II	0	CR	711
25	Pre-B-ALL	2CR	HLA-sib	BM	Bu/Cyc/Eto	MC	0	0	Relapse	174 (†)
26	Pre-B-ALL	1CR	HLA-sib	BM	Bu/Cyc/Eto	DC	IV	extensive	TRM	322 (†)
28	SAA	n.a.	HLA-sib	BM	Cyc+ATG*	MC	0	0	CR	664
30	FA	SAA	MUD	BM	Flu/Cyc/Campath/ATG*	MC	0	0	CR	544
32	LCH	SF	MUD	BM	Flu/Mel/Campath*	MC	0	0	Non-engraftment	370 (†)
33	AML (M1)	1CR	HLA-sib	BM	Bu/Flu/Mel/ATG	DC	0	n.e.	TRM	57 (†)
34	AML (M2)	1CR	HLA-sib	BM	Bu/Mel	MC	I	0	Relapse	474
42	T-ALL	3CR	HLA-sib	BM	Bu/Cyc/Eto	DC	III	extensive	TRM	116 (†)
46	JMML	n.a.	MUD	PB	Bu/Cyc/Mel/ATG	DC	II	extensive	CR	146
48	JMML	n.a.	MUD	BM	Bu/Cyc/Mel/ATG	DC	0	n.e.	CR	81

Chimaerism analysis

Prior to HSCT, blood samples collected from donor and recipient for the determination of the pre-transplant STR profile consisted of fifteen autosomal loci and the Amelogenin gene. In each donor-recipient pair at least one informative allele was identified.

After HSCT approximately 2.7–8 ml freshly obtained peripheral EDTA-blood was collected for chimaerism analysis. Blood samples were taken weekly up to day +50, following once every two weeks until day +100, thereafter once a month during the first year. BM was aspirated regularly 1, 3, 6 and 12 months after HSCT in leukaemic patients. In patients with non-malignant disorders BM was examined only in case of clinical emergency.

Genomic DNA was extracted from whole blood leukocytes using Qiagen DNA extraction kit (QIAmp DNA mini kit; Qiagen, Germany). Prior to STR amplification, all the DNA samples were quantified using BioPhotometer (Eppendorf, Germany). Then, the quantified samples were diluted to the optimal working concentration (15). Pre-transplant DNA obtained from peripheral blood of each recipient and donor pair were amplified with the AmpFlSTR Identifiler PCR Kit (Applied Biosystems, USA) that contained 16 STR markers (D8S1179, D21S11, D7S820, CSF1PO, D3S1358, TH01, D13S317, D16S539, D2S1338, D19S433, vWA, TROX, D18S51, D5S818, FGA) and Amelogenin gene fragment (Amel). The fluorescent PCR products were visualized in an ABI PRISM 310 Genetic Analyzer (Applied Biosystems, USA). Results were analysed using GeneScan 3.1 software and then transferred to Genotyper 2.5 software. For each donor and recipient pair informative alleles that allowed an unequivocal distinguishing of the donor profile from the recipient one were selected. The calculation of the amount of recipient's DNA in the post-transplant sample was performed using special formula (16).

Statistical analysis

The data were analysed using the statistical software package SPSS 13.0. A significance level of 0.05 was assumed for all the statistical tests. Categorical variables in the DC- and MC-groups were compared using Fisher's exact test or Chi-square test for trend. Quantitative variables of the two independent groups were compared using the Mann-Whitney test. The survival estimations in both groups were calculated using the Kaplan-Meier product limit method. The differences between the two groups were compared by the log-rank test.

RESULTS

Chimaerism kinetics and clinical patterns

After the disease-specific conditioning 9 out of 19 patients (47.4%) developed full DC, 10 of 19 patients (52.6%) showed MC (Table 2). Analysis of chimaerism kinetics revealed stable and increasing pattern of MC.

Stable long-lasting MC (Fig. 5) was found in three patients with non-malignant disorders (UPN 3, 28 and 30, see Table 1). This pattern of MC appeared to be associated with a favourable prognosis resulting in a continuous complete remission without any sign of chronic GvHD. Donor compartment in the whole blood leukocytes fluctuated from 80 to 98% donor cells and did not require any modification of immune therapy.

Two patients with non-malignant disorders (UPN 16 and 32) showed increasing MC that caused rapid decrease of the donor compartment followed by the transplant rejection. Both patients received their second graft from the same donor leading to the different outcome: one of them engrafted successfully (UPN 16) with total conversion to the full donor chimera. The patient was

Table 2. **Clinical parameters of the patients according to their chimeric state**

	DC (n = 9)	MC (n = 10)	p-value
Frequency (%)	47.4	52.6	
Underlying disorder			
malignant	9	5	0.033[a]
non-malignant	0	5	
Conditioning			
myeloablative	9	5	0.033[a]
non-myeloablative	0	5	
Donor			
HLA-identical sibling	7	8	1.0[a]
MUD	2	2	
Stem cell source			
BM	6	7	1.0[a]
PB	3	3	
CD34 x10^6/kg cells per recipient BW (mean rank [95% CI])	9.67[1.497-6.832]	10.3[2.220–7.948]	0.842 [b]
aGvHD			
0	3	8	0.064c, [1)]
I–II	3	2	
III–IV	3		
cGvHD			
0	3	8	0.035c, [2)]
local		2	
extensive	3		
not evaluable*	3*		
Transplant related mortality (%)	44.4 (4/9)	0	0.049[d]
Transplant rejection (%)	0	20.0 (2/10)	0.185[d]
Leukemic relapse (%)	0	50.0 (5/10)	0.002[d]
Continuous complete remission (%)	55.6 (5/9)	44.4 (4/10)	0.718[d]
Follow-up after HSCT (mean rank [95% CI])	8.0[75.13–747.09]	11.8[301.54–1024.86]	0.156 [b]

[a] Fisher Exact Test; [b]Mann-Whitney Test; [c]Exact Test (Monte-Carlo-Simulation); [d]Log-Rank Test.

[1)] $\chi^2 = 5.435$; df = 2; [2)] $\chi^2 = 6.691$; df = 2.

* – two of three patients deceased before day +100 after HSCT, i. e. before the cGvHD became evaluable; one patient had insufficient follow-up of less than 100 days.

Abbreviations (see also abbreviations of the whole article): aGvHD – acute GvHD; BW – body weight; cGvHD – chronic GvHD; CI – confidence interval.

in complete remission during the last follow-up. In the other one (UPN 32), the second conditioning could not overcome the host haematopoiesis that resulted in the persistent MC and the second graft failure (Fig. 6). Finally, the patient developed a secondary AML and died.

None of the five leukaemic patients who were found to be mixed chimera (UPN 5, 7, 11, 25 and 34) developed stable MC. All of them showed an increasing MC pattern (Fig. 7). Following conditioning and stem cell infusion all these patients engrafted successfully with 100 percent DC documented by chimaerism analysis. However, recovery of the host malignant cells resulted in the MC that led to the decrease of the donor fraction and subsequent BM relapse. Median time to the detection of MC and the relapse was 134 days ranging from 50 to 400 days after HSCT. All but one patient (UPN 34) received donor lymphocyte infusion; however, it could not arrest the disease progression. In all the patients an attempt of alternative chemotherapy was tried that could delay the lethal outcome in some way. At the time of the evaluation only one of the relapsed patients (UPN 34) remained alive.

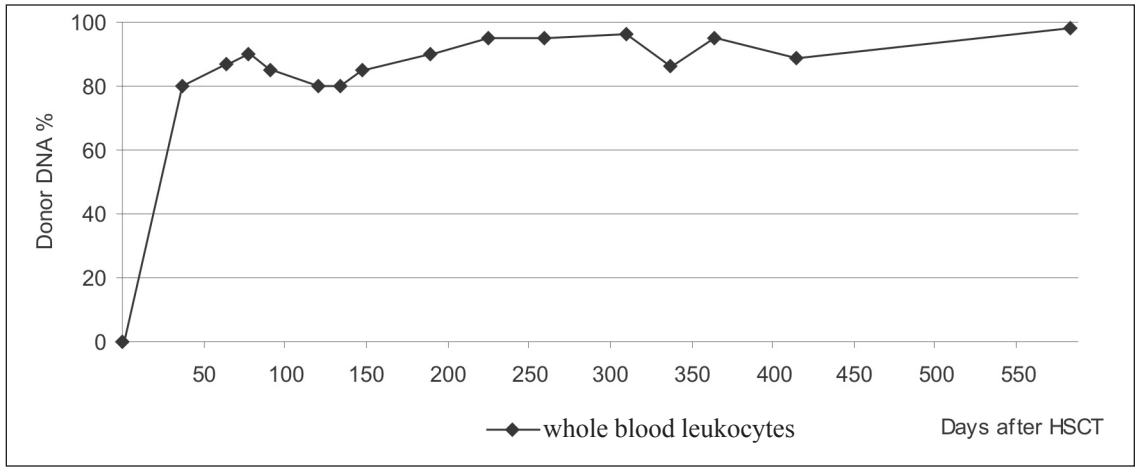

Fig. 5. UPN 28 (see Table 1): stable long-lasting MC

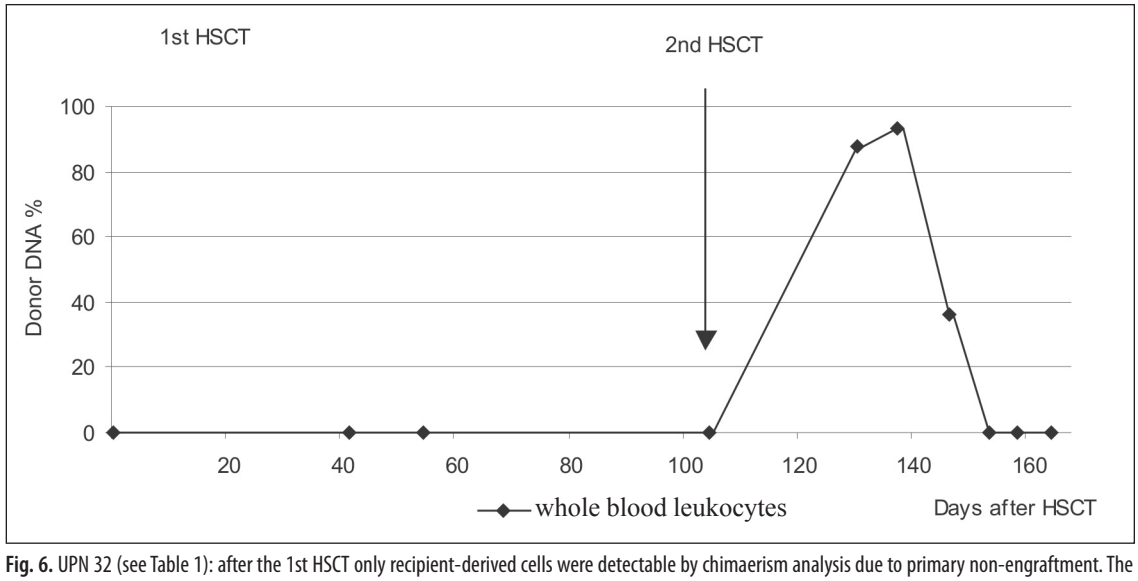

Fig. 6. UPN 32 (see Table 1): after the 1st HSCT only recipient-derived cells were detectable by chimaerism analysis due to primary non-engraftment. The 2nd HSCT from the same donor led to a transient MC followed by the prompt conversion to the full recipient chimaerism as a consequence of the transplant rejection

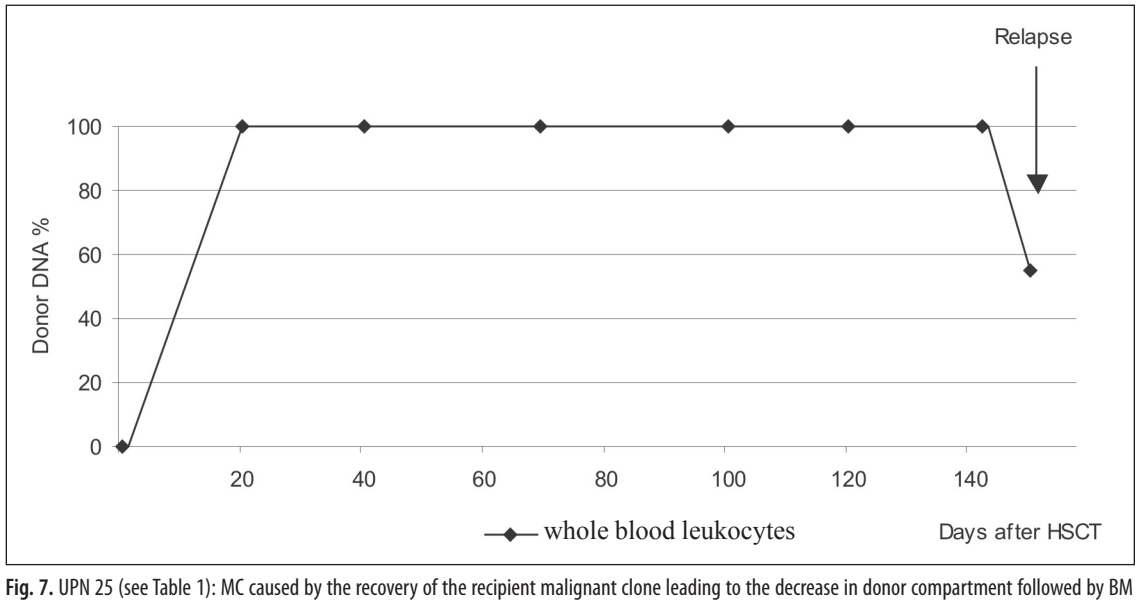

Fig. 7. UPN 25 (see Table 1): MC caused by the recovery of the recipient malignant clone leading to the decrease in donor compartment followed by BM relapse on day +150 after HSCT

Comparison of pre-transplant characteristics and post-transplant events in patients with DC and MC

Pre-transplant characteristics of the patients according to their chimeric state and post-transplant events are summarized in Table 2. All the five patients with non-malignant disorders revealed MC ($p = 0.033$) that seemed to be attributable to the non-myeloablative conditioning ($p = 0.033$) applied to this cohort (Table 1). All the children with malignant disorders received a myeloablative conditioning; then, most of them (9/14) became full donor chimera. Donor type and stem cell source did not differ significantly in both patients' groups ($p = 1.0$ for both variables). Median stem cell dose was higher in the MC-group (4.83×10^6 CD34/kg recipient body weight) than in the DC-one (2.50×10^6 CD34/kg recipient body weight) by the comparable use of BM and PB stem cells.

Children with DC were far more affected by acute and chronic GvHD than those with MC ($p = 0.064$ and $p = 0.035$, respectively). The majority of the MC-patients (8/10) had no signs either of acute or chronic GvHD, 2 out of 10 developed only a mild form (acute GvHD grade I–II and local chronic GvHD). Severe form of GvHD (acute GvHD grade III–IV and extensive chronic GvHD) was observed exclusively in the DC-group. As a consequence, the transplant related mortality reached 44.4% and was significantly higher ($p = 0.049$) in the donor chimera patients comparing with non-toxic death in those with the mixed chimera.

The principal event in the MC-group was transplant rejection and leukaemic relapse. Graft rejection occurred in 2 of 10 patients with MC (UPN 16 and 32 discussed above) vs. none in the DC-group ($p = 0.185$). In patients with malignant disorders MC was strongly associated with the relapse of leukaemia ($p = 0.002$). RFS was found to be unequivocally dependent on the chimeric state (Fig. 8A). Recurrence of leukaemia was the main event in the MC-group meanwhile the DC-patients succumbed mostly to the toxic complications. As a consequence, the EFS (Fig. 8B) and the OS (Fig. 8C) in the leukemic patients did not differ significantly ($p = 0.109$ and $p = 0.653$, respectively). The same trend was obtained for all the patients analysed: the EFS (Fig. 9A) and the OS (Fig. 9B) of the DC- and MC-patients did not differ significantly ($p = 0.435$ and $p = 0.601$, respectively).

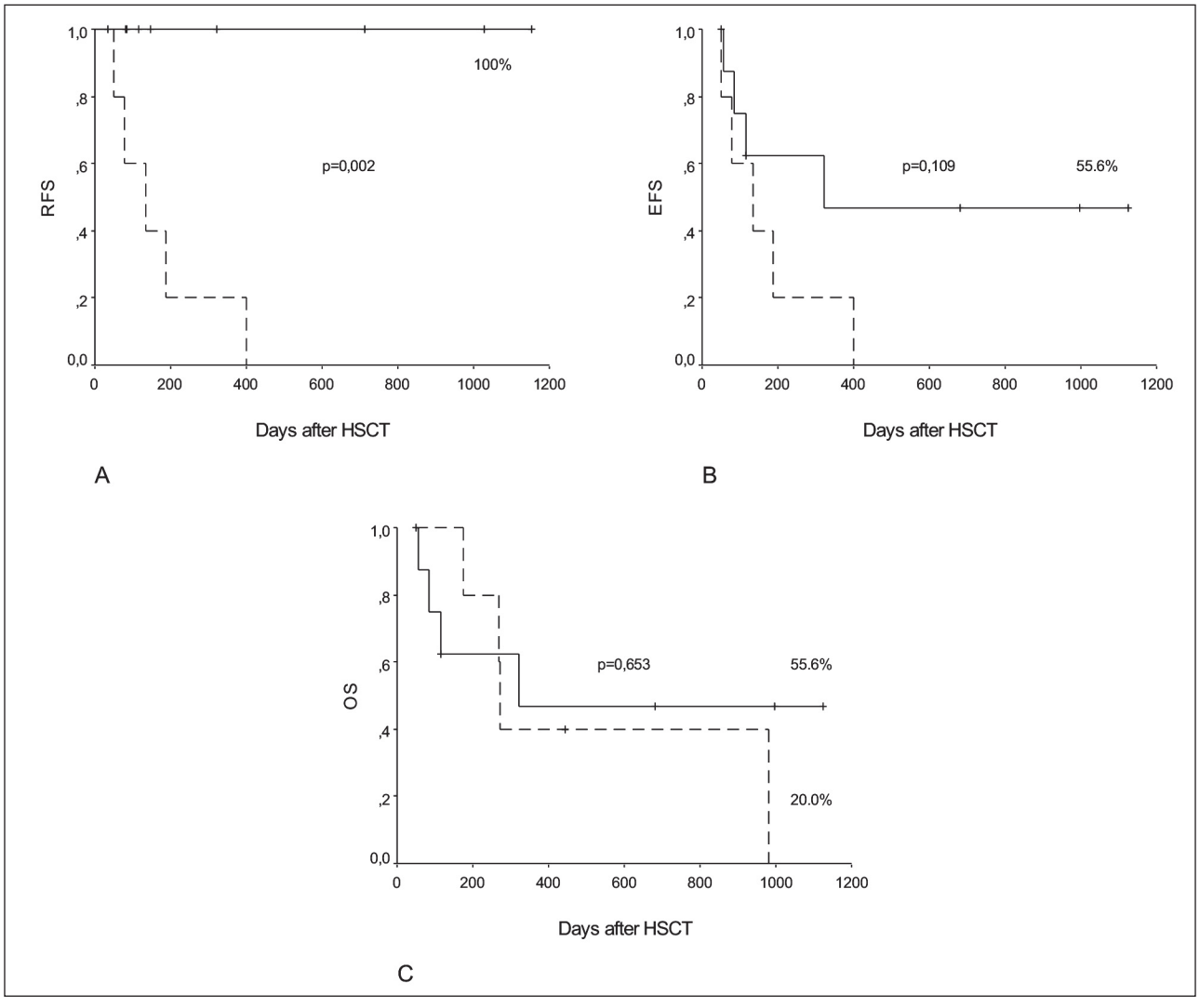

Fig. 8. Kaplan–Meier survival estimation at 3 years of patients with leukemia according to the chimeric state (n=14): —— DC (n = 9), – – – MC (n = 5). A. RFS: DC – 100%, MC – 0; B. EFS (event defined as relapse or transplant related mortality): DC – 55.6%, MC – 0; C. OS: DC – 55.6%, MC – 20.0%

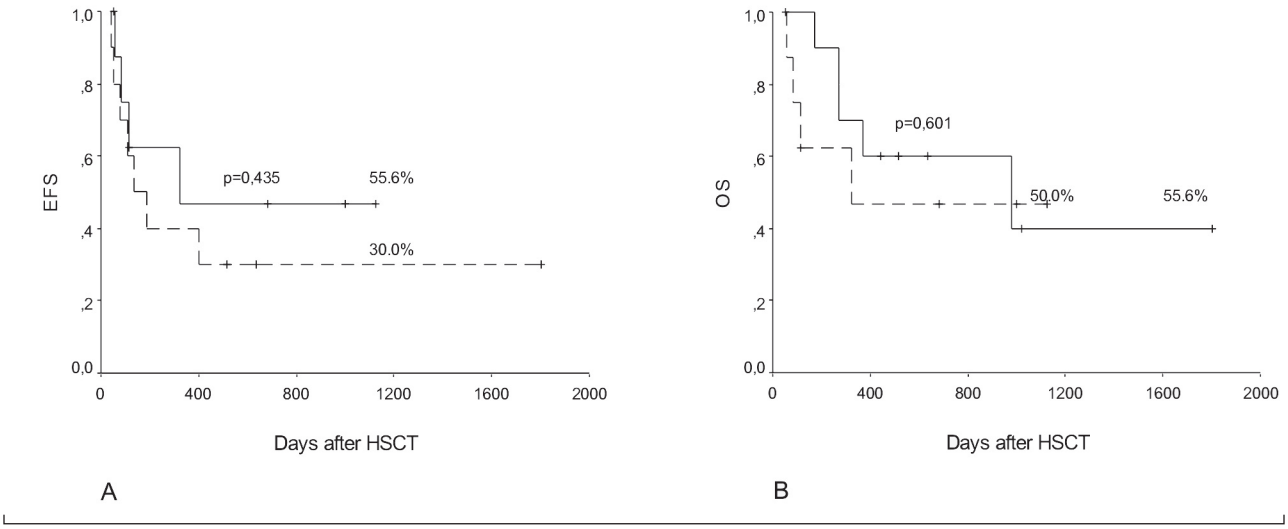

Fig. 9. Kaplan–Meier survival estimation at 3 years of all the patients according to the chimeric state (n = 19): —— DC (n = 9), – – – MC (n = 10). A. EFS (event defined as relapse, transplant rejection or transplant related mortality): DC – 55.6%, MC – 30.0%; B. OS: DC – 55.6%, MC – 50.0%

DISCUSSION

The aim of the study was to analyse the chimaerism kinetics in the Lithuanian paediatric patients after allogeneic HSCT. The peculiarity of the reviewed cohort is a relatively small number of patients and heterogeneity of the disease spectrum. Modest transplant activity reflects scanty paediatric population in a small country. In comparison with other European countries that have comparable number of inhabitants, for instance with Ireland (http://www.census.gov), the number of childhood allogeneic HSCT in Lithuania is significantly lower (2, 17). This could be explained by the decrease in the paediatric population in our country that dropped down from 824.4 thousands in 2002 till 711.8 thousands in 2006 (www.sts.gov.lt). Another important issue is that, prior to 2005, patients could receive an allogeneic graft only if they had an HLA-identical sibling. Since 2005, transplantation from unrelated donors has become available substantially augmenting the feasibility of the procedure for every child.

In our study, 10 out of 19 patients (52.6%) showed MC. This rate of the MC is higher than the reported one of 33 to 47% in the studies that analysed exclusively leukaemic patients (9, 18–22). As has been mentioned above, the patients' cohort consisted of both malignant and non-malignant disorders. MC is rather commonly found in the non-malignant disorders (23–27) perhaps due to more extensive use of non-myeloablative conditioning regimens. The same relationship between non-malignant disorder, non-myeloablative conditioning and MC was confirmed in our patients (p = 0.033). This could explain the higher MC frequency in the described population.

On the other hand, MC was found to be strongly associated with leukaemic relapse (p = 0.002) that confirms the data of the other studies (19, 28). Given 5 relapses out of 14 patients with haematological malignancies (Table 1), a 3-year estimation of RFS was 64.3%. In other studies, a 3-year RFS for childhood ALL fluctuated from 30 to 54% (29, 30), the same outcome for AML at 2 years was 69% (31). Thus, our relapse rate after HSCT remained within the reported range. This is a rather gratifying circumstance as all of the reviewed ALL-patients were conditioned without total body irradiation that remains still unavailable for the Lithuanian patients. In childhood ALL irradiation-based preparative regimens were recognized to be more effective in terms of EFS (defining relapse as event) than those based on busulfan (32, 33). Therefore, they are widely used in the European paediatric centres as a standard conditioning for ALL.

In terms of overall survival, chimeric state did not appear to have any relevance either in malignant setting (p = 0.653) or in the whole patients' cohort (p = 0.601). However, there was a clear difference in the causes of death: in the MC-group transplant rejection and leukaemic relapse were crucial events that compromised the OS (Figs. 8B and 9A). Whereas in the DC-group the major cause of death was transplant-related mortality as a consequence of GvHD. In our study both acute and chronic GvHD developed more frequently in patients with DC (p = 0.064 and p = 0.035, respectively) as well as transplant-related mortality was found to be significantly associated with DC (p = 0.049). Close relationship between survival and GvHD was confirmed in another study: Zecca et al. (34) reported the transplant-related mortality rate of 64% in patients with extensive chronic GvHD. The evidence that the risk of GvHD is much lower in case of MC, especially in T-cell subset, came from other numerous studies (28, 35–37).

The univariate analysis of pre-transplant variables revealed that only non-malignant disorders and non-myeloablative conditioning were important for the development of MC as discussed above. In our study donor type, stem cell source and CD34 cell dose did not appear to have any impact on the chimeric state. Lack of evidence was probably attributable to the mixed study population. Other reports favoured the development of MC after the use of BM for haematological malignancies (38, 39) as well as in patients with non-malignant disorders (W. Ebell and M. Nagy, personal communication, publication in

preparation). After non-myeloablative transplantation, donor type failed to demonstrate any impact on the level of chimaerism (40) whereas higher CD34 cell dose was indeed associated with better engraftment and higher DC level (41–43).

CONCLUSIONS

Currently, the present study is the first one that studied chimaerism kinetics after allogenic HSCT in Lithuanian paediatric patients. The rate of MC in the analysed cohort was found to be higher than the one reported by other study groups. Non-malignant disorders and non-myeloablative conditioning were important for the development of MC, whereas other pre-transplant variables (donor type, stem cell source and CD34 cell dose) did not appear to have any impact on the chimeric state. Higher rate of MC in Lithuanian children did not affect the transplant results in terms of survival. Thus, our data could be considered as indirect evidence that paediatric transplant service in Lithuania is consistent with the current practice in Europe (44).

Abbreviations

ALL	acute lymphoblastic leukaemia
AML	acute myeloid leukaemia
BM	bone marrow
CML	chronic myeloid leukaemia
DC	donor chimaerism
DNA	deoxyribonucleic acid
EDTA	ethylenediaminetetraacetic acid
EFS	event-free survival
GvHD	graft-versus-host disease
HLA	human leukocyte antigen
HSCT	haematopoietic stem cell transplantation
JMML	juvenile myelomonocytic leukaemia
MC	mixed chimaerism
MUD	matched unrelated donor
OS	overall survival
PB	peripheral blood
PCR	polymerase chain reaction
RFS	relapse-free survival
SAA	severe aplastic anaemia
STR	short tandem repeats
UPN	unique patient number

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CHIMERIZMO ANALIZĖ PO ALOGENINĖS KRAUJODAROS KAMIENINIŲ LĄSTELIŲ TRANSPLANTACIJOS LIETUVOS VAIKAMS

S a n t r a u k a

Įvadas. Alogeninė kraujodaros kamieninių ląstelių transplantacija (KKLT) vaikams Lietuvoje pradėta atlikti nuo 2002 m. vasario mėnesio. KKLT sėkmei ir rezultatams didžiulę įtaką turi chimerizmo (donoro ir recipiento ląstelių santykio) kinetika, todėl chimerizmo tyrimas yra vienas pagrindinių transplantato prigijimo rodiklių.

Tikslas. Tyrimo tikslas – išanalizuoti chimerizmo kinetiką po alogeninės KKLT vaikams, kuri buvo atlikta Vilniaus universiteto vaikų ligoninėje. Chimerizmo kinetika lyginta su klinikine eiga, taip pat įvertinta prieštransplantacinių veiksnių įtaka chimerinei būklei.

Pacientai ir metodai. Ištirta 19 vaikų su piktybinėmis ir nepiktybinėmis kraujo ligomis. Ligoniams buvo persodintos pagal žmogaus leukocitų antigenus tapačių gimininių ir negimininių donorų kraujodaros kamieninės ląstelės. Chimerizmas tirtas DNR polimorfiniais žymenimis nustatant nefrakcionuotus periferinio kraujo leukocitus.

Rezultatai. Visiškas donoro chimerizmas (DC) rastas 47,4% (9 iš 19) ligonių, mišrus chimerizmas (MC) – 52,6% (10 iš 19) ligonių. Vaikams, sergantiems nepiktybinėmis kraujo ligomis, stebėtas stabilus ir didėjantis MC, tuo tarpu sergantiems leukemija nustatytas tik didėjantis MC. MC išsivystyti turėjo reikšmės nepiktybinė kraujo liga ($p = 0,033$) ir nemieloabliacinė paruošiamoji chemoterapija ($p = 0,033$). Dviem iš penkių vaikų, sergančių nepiktybinėmis kraujo ligomis, MC sukėlė transplantato atmetimą. Piktybinių ligų grupėje MC buvo riekšmingai susijęs su leukemijos recidyvu ($p = 0,002$). Šios pagrindinės komplikacijos iki 50,0% sumažino bendrą ligonių su MC išgyvenamumą. Tuo tarpu pagrindinė ligonių su DC mirties priežastis buvo toksinės komplikacijos ($p = 0,049$), kurios lėmė panašų bendrą išgyvenamumą (55,6%).

Išvados. Chimerizmo kinetika neturėjo įtakos ligonių išgyvenamumui be komplikacijų ($p = 0,435$) ir bendram išgyvenamumui ($p = 0,601$). Tyrimo rezultatai iš esmės atkartoja ankstesnių studijų, nagrinėjusių chimerizmo kinetiką, duomenis. Taigi galima teigti, kad vaikų KKLT tarnyba Lietuvoje atitinka šiuolaikinius Europos pediatrinės KKLT standartus.

Raktažodžiai: chimerizmas, alogeninė kraujodaros kamieninių ląstelių transplantacija, polimorfiniai DNR žymenys