soho2023
ELEVENTH ANNUAL MEETING

MOLECULAR KARYOTYPE OF TUMOR CELLS IN PH-NEGATIVE B-ACUTE LYMPHOBLASTIC LEUKEMIA (B-ALL) IN ADULT PATIENTS

Abdulpatakh Abdulpatakhov MD[1], Natalya Risinskaya MD, PhD[1], Olga Aleshina MD, PhD[1], Maria Kislitsyna Md, PhD[1], Anna Yushkova MD[1], Olga Dubova MD[1], [2], Anastasia Vasileva MD[1], Ekaterina Kotova MD[1], Galina Isinova MD, PhD[1], Tatiana Obukhova MD, PhD[1], Hunan Julhakyan MD, PhD[1], Andrey Sudarikov MD, PhD[1], Elena Parovichnikova MD, PhD[1]

1. National Medical Research Center for Hematology, Moscow, Russian Federation.
2. I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation.

INTRODUCTION

Tumor cells of the patients with Ph – negative B-ALL may have a variety of genetic lesions. New diagnostic methods, such as chromosomal microarray analysis (CMA), allow searching for new molecular factors related to pathogenesis and associated with the disease prognosis.

METHOD

CMA (GeneChip System 3000) of the tumor cells was performed for the patients with de novo Ph negative B-ALL, admitted to the National Medical Research Center for Hematology (Moscow, Russia) from 2021 to 2023.

AIM

To appreciate the landscape of tumor molecular karyotypes in a diagnosis of Ph-negative B-ALL.

RESULTS

Of 21 patients, only 3 (pts. № 1, 12, 15) had a normal molecular karyotype. Eleven (53%) showed signs of tumor heterogeneity (5 (24%) patients had multiple duplications, 2 (10%) had deletions, and 4 (19%) had both deletions and duplications). Homozygous deletion of 9p21.3 (*CDKN2A* gene) was established for 4 patients. Early lethality was noted for 1 patient (№ 21) with multiple losses and gains. Two patients (№ 8,10) (both with cnLOH, one with deletion of 9p21.3) had a refractory disease course. After 2 induction courses according to the protocol, of 18 patients: 10 (55%) had minimal residual disease (MRD)- remission and 8 (45%) MRD + remission. Tumor heterogeneity was found in 4 (50%) of 8 patients from the MRD + group vs 6 (60%) of 10 in the MRD - group. However, statistical significance was not reached (P=0.18). For more details look at the table.

- MRD negative patients
- MRD positive patients
- non tumor heterogeneity
- tumor heterogeneity

Chromosome	1.F 31 +	4.F 33 +	5.F 34 +	6.M 35 +	12.F 36 +	15.M 19 +	16.M 19 +	18.F 27 +	2. F 26 -	3. F 53 -	7. F 24 -	9. F 28 -	13. M 20 -	14. M 21 -	17. M 22 -	19. M 44 -	22. F 44 -	23. F 38 -	10. M 53 R trans AML	8.M 40+ R, D	21. F 46 D
1p		1p21.2p21.1x2 hmz																		1p31.1p31.1x2 hmz	1p36.13p34.31x1 [0.2]
1q								1q21.1q23.3x3 [0.7] 1q23.3q43x5 [0.5], 1q43q44x4 [0.6]												1q23.3q44x3
2p										2p16.3x1											
2q			2q24.1q24.1x2 hmz																2q36.3q37.1x2 hmz		
2chr											(2)x3 [0.1]				(2)x1	(2)x1					
3p		3p21.1p14.2x2 hmz, 3p22.1p21.31x2 hmz		3p21.31x1							3p26.3p12.2x1 [0.3], 3p12.1p11.1x2 hmz			3p26.3p22.3x3[0.1] 3p21.31p21.1x2 hmz							
3q		3q25.31q26.1x2 hmz,									3q25.33q29x3 [0.3]										3q13.12q13.2x1 [0.5]
3chr			(3)x1 [0.19]												(3)x1	(3)x1					
4q		4q34.3q34.3x2 hmz	4q31.3q32.1x1 [0.2]													4q26q26x2 hmz			4q12q13.2x2 hmz		4q21.22q28.1x1 [0.2] 4q35.1q35.2x1 [0.2]
4chr							(4)x3					(4)x5	(4)x3	(4)x3 [0.72]	(4)x1			(4)x3			
5p		5p13.1q11.2x2 hmz														5p13.2p13.1x1					
5q										5q35.2q35.3x2 hmz										5q23.1q23.1x2 hmz	5q11.2q12.1x1 [0.2],
6p		6p22.3p22.3x2 hmz																			
6q				6q16.1q22.1x1							6q16.3q24.3x1 [0.6]		6q15q23.1x1[0.36]								6q11.1q21x3 [0.5] 6q22.32q22.33x2 hmz 6q24.3q25.1x1 [0.5], 6q25.3q27x1 [0.5],
6chr		(6)x3 [0.14],					(6)x3					(6)x3		(6)x3 [0.69]				(6)x3			
7p										7p12.3p12.1x1											
7q			7q31.2q31.31x2 hmz														7q35q36.2x1 [0.3]				
7chr			(7)x1 [0.19]												(7)x1	(7)x1					
8p		8p23.1p22x2 hmz,																			
8q																					8q11.1q11.21x2 hmz,
8chr			(8)x3 [0.31]							(8)x3			(8)x3					(8)x3			
9p				9p24.3x3				9p24.3p12x1 [0,31],		9p24.3p21.3x2 hmz 9p21.3x0, 9p21.3p13.1x2 hmz,			9p21.3x0 9p21.3p21.2x1				9p21.3p21.2x1 [0.4]	9p24.3p13.1x2 hmz 9p21.3x1	9p24.3p13.2x1 hmz 9p21.3p21.3x0 [0.5]	9p24.3p24.2x0 [0.3] 9p24.1p21.3x1,9p21.3p21.3x0 [0.3], 9p21.3p11.2x1	
9q		9q22.31q31.1x2 hmz								(9q)x4			9q22.33q31.1x1,								9q21.11q34.3x3
9chr			(9)x1 [0.19]								(9)x1 [0.21]			(9)x3 [0.42]	(9)x1						
10chr			(10)x3 [0.29]				(10)x3					(10)x3,		(10)x3				(10)x3			
11p				11p14.3p12x1 11p11.2q12.1x1								11p11.2p11.12x2 hmz,									
11q		11q22.3q23.2x2 hmz		11q14.2q14.3x1, 11q22.1q23.3x1,11q23.3q24.1x1, 11q24.1x1									11q22.3x1			11q13.3q25x3					
11chr											(11)x1 [0.3]										
12p				12p13.31x3							12p13.33p13.2x1 [0.22] 12p11.23q22x3 [0.3],					12p13.33p11.22x1					
12q											12q22q24.33x1 [0.2],										
12chr															(12)x1						
13q													13q14.2q31.1x1			13q12.11q22.3x1 13q22.3q34x1 [0.2]					13q12.11q12.12x1 [0.5],13q13.3q31.1x1 [0.5]
13chr															(13)x1						
14q					14q31.2q32.33x3													14q23.1q23.2x2 hmz			
14chr			(14)x3 [0.3]									(14)x3	(14)x3	(14)x3				(14)x3			
15chr			(15)x1 [0.2]								(15)x1 [0.72]					(15)x1					
16chr			(16)x1 [0.19]												(16)x1	(16)x1					
17p											17p13.3q21.31x1 [0.2]										
17q										17q11.2q11.2x2 hmz	17q21.31q25.3x2 hmz [0.5]										
17chr							(17)x3					(17)x3		(17)x3	(17)x1	(17)x1		(17)x3			
18p																					18p11.32p11.31x1 [0.5]
18q																18q11.2x3					
18chr							(18)x5					(18)x3	(18)x3	(18)x3				(18)x3			
19p				19p13.3x1				19p13.3x1						19p13.3p13.3x1 [0.4], 19p13.2p13.12x3 [0.3]							19p13.3x1
20chr			(20)x1 [0.17]												(20)x1	(20)x1					
21q											21q22.12q22.3x3 [0.3]										
21chr			(21)x3 [0.31]				(21)x3					(21)x5	(21)x3	(21)x5				(21)x5			(21)x3
22chr										(22)x3	(22)x3 [0.1]					(22)x1					
Xp											Xp22.33p11.3x1 [0.2] Xp11.3q28x1 [0.5]										
Xchr		(X)x3 [0.6]	(X)x1 [0.2]				(X)x2 [0.78]			(X)x3		(X)x3	(X)x2 [0.83]	(X)x2 [0.81]				(X)x3			(X)x1 [0.1]
Ychr																(Y)x0 [0.8]					

CONCLUSIONS

Thus, in 53% of patients, tumor heterogeneity was established at the onset of the disease. When comparing groups of patients with and without signs of tumor heterogeneity, there were no significant differences in achieving MRD- remission. However, all patients who did not achieve remission of the disease had changes in DNA copy number. The significance of the identified changes is to be assessed with a longer follow-up.

ACKNOWLEDGEMENTS

The research was supported by Russian Science Foundation (RSF project No. 23-25-00490)

CONTACT INFORMATION

Hunan Julhakyan

oncohematologist@mail.ru