soho2023
ELEVENTH ANNUAL MEETING

MICROARRAY MOLECULAR KARYOTYPE VS STANDARD CYTOGENETIC ANALYSIS IN PATIENTS WITH ACUTE MYELOID LEUKEMIA (AML) WITH INV(16)

Dmitry Bessmertnyy MD, Natalya Risinskaya MD, PhD, Anastasiya Kashlakova MD, Irina Lukianova MD, PhD, Zalina Fidarova MD, PhD, Mariya Kislitsyna MD, PhD, Tatyana Obukhova MD, PhD, Hunan Julhakyan MD, PhD, Andrey Sudarikov MD, PhD

National Medical Research Center for Hematology, Moscow, Russian Federation

INTRODUCTION

The landscape of copy number alterations (CNA) and copy-neutral loss of heterozygosity (cnLOH) is important for understanding the nature of myeloid neoplasms. AML with 16th chromosome inversion is associated with a good prognosis. Most patients achieve full remission after the first (standard) chemotherapy course. The mechanisms of chemosensitivity in these cases are not yet known, and furthermore, relapses can still occur. The diagnostic routine includes standard cytogenetic analysis (CA) and fluorescence in situ hybridization (FISH) to reveal structural and copy number aberrations. To test for copy-neutral loss of heterozygosity (CN-LOH), chromosomal microarray analysis (CMA) should be used.

AIM

To compare CA and FISH with CMA in AML inv(16) patients.

METHOD

Two AML patients with inv(16) diagnosed and treated now at the National Medical Research Center for Hematology (Moscow, Russia) were randomly selected. CA showed standard female karyotype in the first patient and male karyotype with trisomy22 in the second. Inversion of 16th chromosome in both patients was revealed by FISH analysis. No mutations in *FLT3*, *NPM1*, and *CEBPa* genes were found in both patients. Both received “7+3” (cytarabine 200 mg/m2 day 1-7, daunorubicin 60 mg/m2 day 1-3) as the first course of chemotherapy. Immunophenotypical remission was achieved in both patients, although chimeric transcript *CBFB*::*MYH11* was still detectable. DNA extracted from bone marrow samples during primary diagnosis was used for CMA performed on GeneChip System 3000 platform.

RESULTS

For the first patient, molecular karyotype with additional aberrations was found: gain 3q12.2 with ADGRG7 and TFG genes involved, loss 7p22.3, cnLOH 15q24.1q24.2. It should be noted that ADGRG7 and TFG gene overexpression has been observed previously in many solid tumors. Second patient also had additional aberrations: cnLOH 1p13.1p12, 2q33.3q34, 3p21.31p21.1, loss 3p13, cnLOH 3p12.2p11.2,11q13.2q25 [0.5], 12p11.22q12, gain 22. More CN-LOH were found in the second patient, but the chemosensitivity was similar to that of the first patient.

CONCLUSIONS

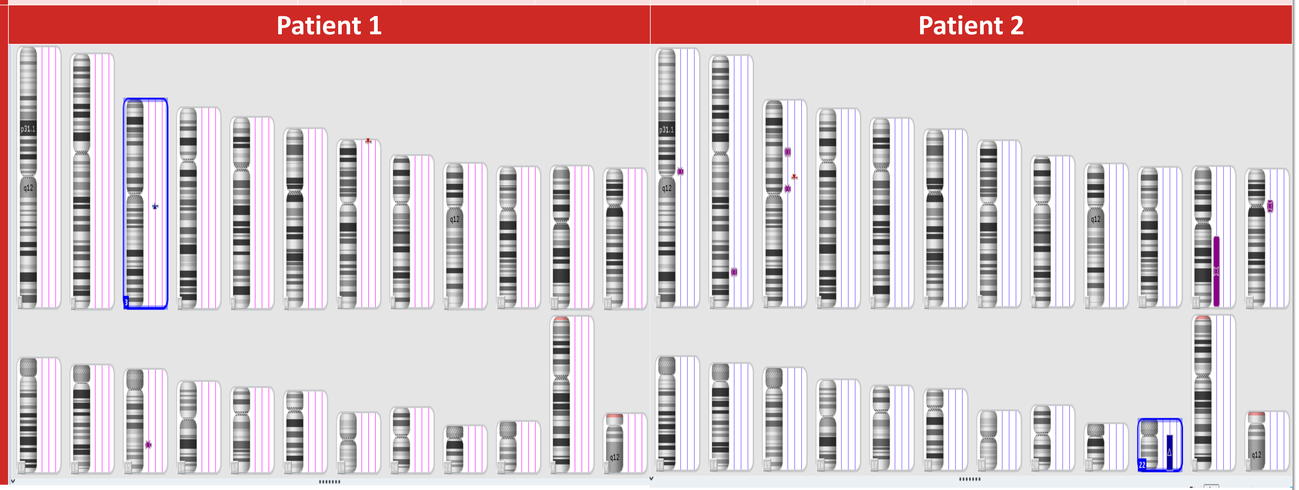
In AML patients with inv(16), CMA can reveal additional CN-LOH areas, small deletions, and duplications. Performing CMA on a large patient cohort might identify possible molecular markers associated with chemosensitivity in patients with AML inv(16).

CONTACT INFORMATION

Hunan Julhakyan

oncohematologist@mail.ru

		Patient 1			Patient 2							
CN state		3.0	1.0					1.0		mos		3.0
Type		Gain	Loss	LOH	LOH	LOH	LOH	Loss	LOH	LOH	LOH	Gain
Chromosome		3	7	15	1	2	3	3	3	11	12	22
Cytoband	Start	q12.2	p22.3	q24.1	p13.1	q33.3	p21.31	p13	p12.2	q13.2	p11.22	q11.1
	End	q12.2	p22.3	q24.2	p12	q34	p21.1	p13	p11.2	q25	q12	q13.33
Size		153.34	1161.385	3095.934	4166.202	7181.829	8122.338	515.329	4422.084	67883.71	10993.31	34825.10
Marker Count		84	457	748	988	1953	2225	112	877	28475	2794	14623
Gene count		2	22	66	44	56	228	3	9	678	35	632
OMIM Gene count		2	9	45	27	32	147	1	2	399	20	368



Results of chromosomal microarray analysis