A CASE OF ACUTE MYELOID LEUKEMIA WITH COMPLEX KARYOTYPE INVOLVING RING 11 CHROMOSOME

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INTRODUCTION

Acute myeloid leukemia (AML) is a heterogeneous group of diseases. In some cases patients have a satisfactory survival whereas in others the course is with dismal prognosis. Karyotyping is a powerful independent prognostic indicator in this group of diseases. Three subgroups can be distinguished: (i) AML with normal karyotype, (ii) AML with a primary balanced chromosome aberration, and (iii) AML with unbalanced karyotype abnormalities characterized by gains and/or losses of usually larger regions of the genome and no known primary balanced abnormality. Complex karyotypes are defined as 3 or more independent chromosomal abnormalities in one genome. AML patients with such abnormalities are characterized by a low overall response rate, and often relapse after clinical treatment. Here we describe a case with complex karyotype involving uncommon chromosomal abnormalities.

OBJECTIVE

Clarification of the case after relapse with additional immunophenotypic analyses and molecular cytogenetics (FISH).

METHODOLOGY

Survey of medical history, physical examination, laboratory tests, bone marrow immunophenotypic studies and fluorescence in situ hybridization/FISH (cytogenetic analyses).

RESULTS

At diagnosis analysis revealed 23% blasts, positive for CD34, HLADR, CD33 and negative for CD7, CD19 and other. The patient was treated with citarabine/daunorubicine and hematologic remission was achieved after the first cycle. Nevertheless, less than one year, the myelogram depicted blasts and the immunophenotypic study revealed blasts: 71.2% - positive for HLA DR, CD33, CD38, CD117 among others (Figure 1). Molecular analysis was positive for AML-ETO/t(8;21) rearrangement and negative for PML-RARA/t(15;17) and CBFb-MyH11/inv(16)/t(16;16) rearrangements.

The cytogenetic study using GTG banding revealed a complex karytype of 46,XX,r(11),add(12)(p13),der(5?),der(13?)[15] (Figure 2).For further clarification, fluorescence in situ hybridization (FISH) was performed applying whole chromosome probes (wcp) for chromosomes 5, 11, 12, and 13 (e.g Figure 3).The molecular cytogenetic results were as follows: 46,XX,der(5)t(5;13),r(11),der(12)t(12;?)(p13;?)[4];46,XX,der(5)t(5;13),der(11)(qter->p1?1.12::p1?1.12->qter),der(12)t(12;?)(p13;?[4];and 46,XX,der(5)t(5,13),der(11)t11;?)[1].

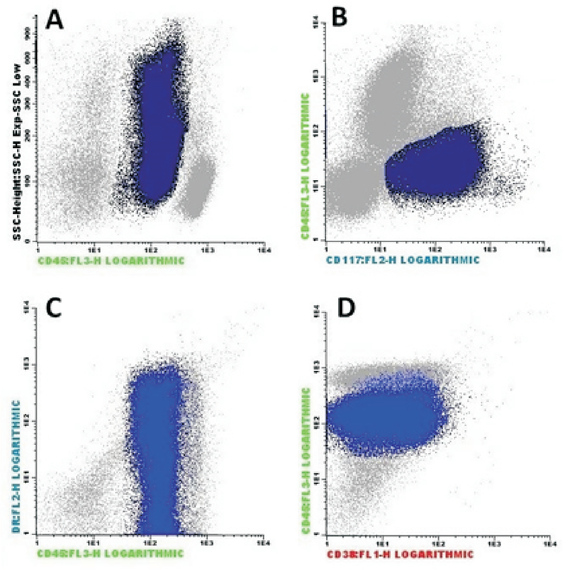

Figure 1: Immunophenotypic study in patient with acute myeloid leukemia (AML). Dot plots revealing 71.2% of blasts (A) positive for (B) CD117 (44.31%), (C) HLA DR (87.12%) and (D) CD38 (80.53%), less than one year of citarabine/daunorubicine treatment and despite of hematologic remission after the first cycle treatment.

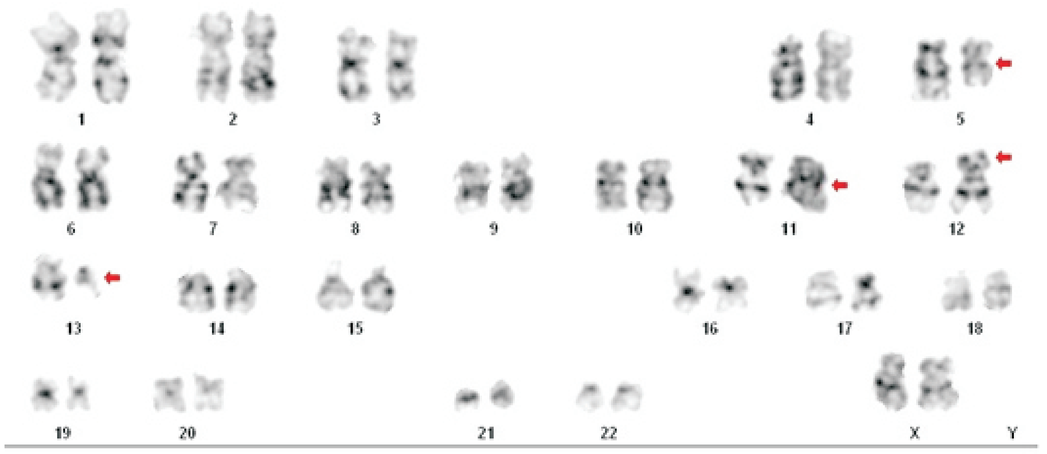

Figure 2: Conventional giemsa trypsin giemsa (GTG)-banding along with molecular cytogenetic techniques is valuable tool in identifying genomic alterations and rearrangements. Our cytogenetic study using GTG banding revealed a complex karyotype involving at least four chromosomes,46,XX,r(11),add(12)(p13),der(5?),der(13?)[15].

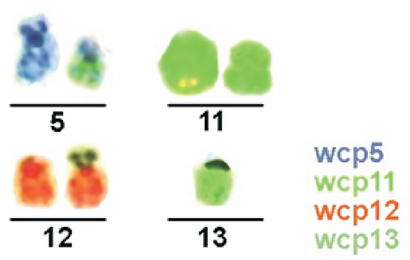

Figure 3: Fluorescence in situ hybridization (FISH) was performed applying whole chromosome probes (wcp) for chromosomes 5, 11, 12, and 13. The images were obtained separately and then captured. This technique showed translocations on chromosomes 5 and 12, and a ring formation in chromosome 11.

CONCLUSION

Molecular cytogenetic studies are suited best for identification and characterization of chromosomal rearrangements in acute leukemia. Ring chromosomes are considered to be rare in hematopoietic cancer, however, with regard to ring chromosome 11, this abnormality was found only in 19 AML patients. Single case reports as well as population studies are necessary to provide further insights into karyotypic changes taking place in human malignancies and obesity.

FINANCIAL SUPPORT: Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ).

KEYWORDS: acute myeloid leukemia, obesity, ring chromosome, fluorescence in situ hybridization.

Projeto Gráfico: Serviço de Edição e Informação Técnico-Científica / INCA