NUMERIC CHROMOSOMAL CHANGES OF THE SMALL ACROCENTRICS IN ACUTE LEUKEMIA

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Abstract

Acute leukemia is a clonal disturbance due to malign transformation of a myeloid or lymphoid progenitor cell, which allows the classification of leukemia in acute lymphoblastic leukemia and acute myeloblastic leukemia.
50 cytogenetic analyses of patients with leukemia with ages between 2 -73 years have been performed in the Cytogenetic laboratory of the University of Medicine and Pharmacy Victor Babes Timisoara during 2004-2009.
The diagnostic cytogenetic analysis has been shown to be an important prognostic factor, capable of predicting remission duration and the therapeutic management. For the confirmation of previous data, CGH may provide useful information regarding the nature of genomic aberrations that take place in cases with complex karyotypes.
Keywords: Small Acrocentrics(21 and 22), chromosomal abnormalities, acute leukemia

Introduction

Acute myelocytic leukemia (AML) and Acute lymphoblastic leukemia (ALL) is characterized by a variety of numerical and structural chromosome aberrations.Gains and losses of whole chromosomes occur frequently in AML and ALL, both as solitary changes, usually found at diagnosis, and as additional aberrations in later disease stages.
Chromosomal abnormalities in neoplastic marrow cells often correlate closely with specific clinical and biologic characteristics of the disease and serve as a tool to predict the clinical outcome and develop effective therapeutic approaches.

Material and method

During the period between 2004 and 2009, in Cytogenetics Laboratory of University of Medicine and Pharmacy "Victor Babes" Timisoara, there were performed 50 cytogenetics tests of the patients with the suspicion of acute lymphoblastic leukemia and acute myeloblastic leukemia. Most of the tests were undertaken before the beginning of the treatment. The patients are represented by children with the age between 2 and 14 years, as well as adults with the age between 20 years and 73 years. The samples were obtained from the bone marrow using the direct method (without cellular cultures) and the indirect method, this method implying cellular cultures with the length of 24, 48, 72 hours. For specimen collection, 1-2 ml of marrow are aspirated aseptically into a syringe coated with preservative-free sodium heparin and transferred to a sterile 15 ml centrifuge tube containing 5 ml culture medium (RPMI 1640, 100 units sodium heparin).For blood specimens, 5 ml are drawn aseptically by venipuncture into a syringe coated with preservative- free heparin. Specimen should be maintained at room temperature and transported in culture medium. To prepare metaphase cells, the sample is exposed sequentially to mitotic inhibitors to accumulate cells in mitosis, hypotonic KCl (0.075M) to swell the cells, and fixative (absolute methanol: glacial acetic acid, 3:1). Slides are prepared by dropping the cell suspension onto precleaned glass microscope slides, and the slides are air dried. The most popular chromosomal banding techniques is trypsin-Giemsa banding.Using this technique, a consistent chromosome banding pattern is induced by exposing cells to a dilute trypsin solution (0,1-0,25 percent), followed by staining in phosphate-buffered Giemsa stain

The assessed metaphases, 20 for each patient, had a proper quality due to the adherence to the protocol. It also was noticed a better dispersion of the chromosomes from the cells with normal karyotype.

Results

The numeric chromosomal changes of the group G chromosomes are the following: totally 21 trisomy as a single anomaly(fig.1); totally 21 trisomy as a collateral anomaly occurred in a case with totally 6,8,19 trisomy and long arm q17 isochromosome(fig.2); 17 trisomy observed in other case(fig.3); totally tetrasomy of chromosome 21 along with 6 trisomy, 19 trisomy, long arm q17 isochromosome(fig.4); totally 22 trisomy as a collateral anomaly along with 15 monosomy and 11q23 deletion(fig.5). 21 trisomy was encountered at the patients with acute lymphoblastic leukemia and 22 trisomy at a patient with acute myeloblastic leukemia.

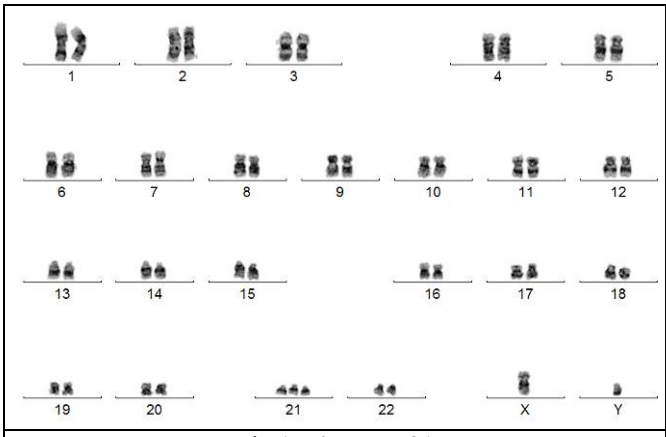

Fig 1- 47,XY,+21

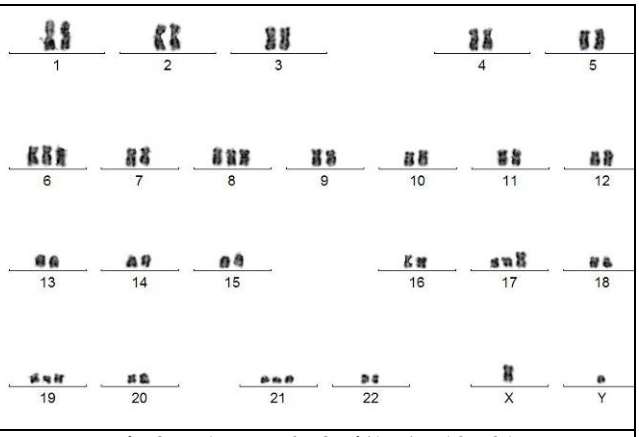

Fig 2 - 51,XY,+6,+8,+i(17q),+19,+21

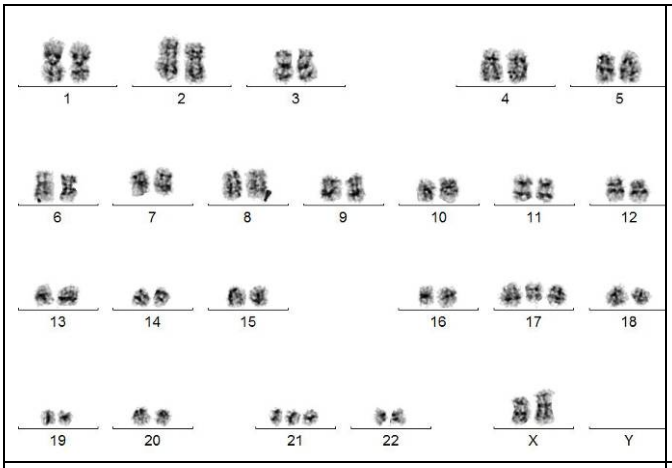

Fig 3 - 48,XX,+17,+21

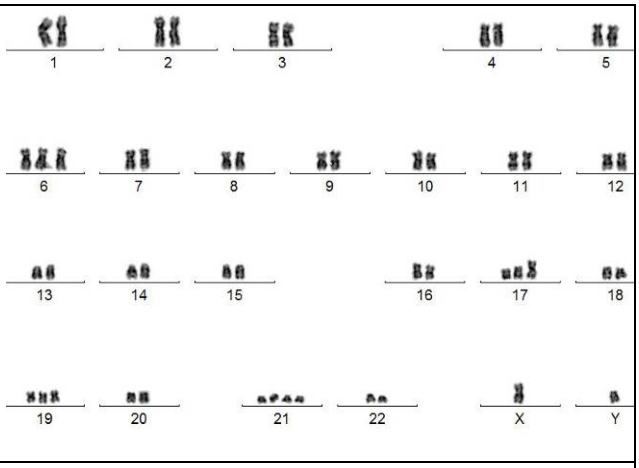

Fig 4 - 51,XY,+6,+i(17q),+19,+21,+21

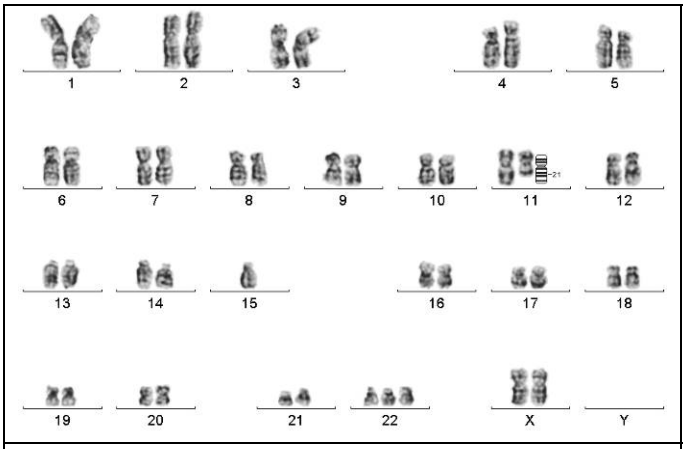

Fig 5 - 46,XX,-15,+22,del11q

Discussions

21 trisomy is more frequently encountered in acute lymphoblastic leukemia, but is also seen in acute myeloblastic leukemia as a single anomaly or as a collateral anomaly without specificity for any FAB subtype. As unique anomaly it occurred in acute lymphoblastic leukemia in our study, while in medical literature it is characteristic for acute myeloblastic leukemia type M7 (megakaryoblastic).

21 tetrasomy was also described in megakaryoblastic leukemia as a clonal anomaly.

22 trisomy was found in our study at a case with acute myeloblastic leukemia, in medical literature this anomaly is found more often at the patients with acute myeloblastic leukemia type M4. It seems that this chromosomal disorder is the cause of the erythropoiesis's decreasing. In 90 percent of the cases it was encountered as a collateral anomaly.

Besides the numeric changes of the 21 and 22 chromosomes, these patients present totally 6, 8, 19, 17 trisomies, as well as 17q isochromosome and 11q deletion.

Totally trisomies frequently encountered in acute lymphoblastic leukemia are: 4, 6, 10, 14, 17, 18, 20, 21. 8 trisomy occurs in acute lymphoblastic leukemia but is more frequent in acute myeloblastic leukemia. 11q23 deletion without rearrangement of the MLL gene is associated with a favorable evolution. 4, 6, 10 and 21 trisomies are markers for a good prognostic along with a good survivorship.

Conclusions

The cytogenetics diagnosis is a prognostic factor with the capacity to predict the remission rate, the length of the remission and the survivorship period, regardless of the haematological, immunological and clinics parameters.

Hyperdiploidia is a disorder frequently encountered in acute lymphoblastic leukemia, the one characterized by more than 50 chromosomes leading to a favorable evolution, while hyperdiploidia with less than 50 chromosomes denotes a poor prognosis. Nevertheless 6 and 21 trisomy indicate a favorable prognosis, 11q23 deletion does not imply the rearrangement of the MLL gene. Even if 8 trisomy is a characteristic of the myeloid disorders, in our study it was encountered in acute lymphoblastic leukemia.

Even if 21 and 22 trisomies are not particularities of any type of acute leukemia, they are frequently encountered.

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