Comparative genomic hybridization (CGH) in detection of chromosomal changes in 120 childhood acute lymphoblastic leukemias. Update of results.

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Introduction

Global chromosomal abnormalities are identified in 55-90 % of childhood acute lymphoblastic leukemia (ALL) depending on the experience of the diagnostic laboratories involved and on the techniques used. The identification of chromosome abnormalities in childhood ALL not only represents an important prognostic and therapeutic factor, enabling to stratify patients into prognostic subgroups, but it also contributes to better understanding of the biological heterogeneity of the disease.

Patients

One hundred and twenty pediatric patients with ALL were included in the study. The patients were diagnosed and treated in four Children Hematological Centres in Prague, Brno, Ostrava and Olomouc between 1997 and 2003.

The cytogenetic examinations of 52 patients were performed in the centres in Prague and Brno, while the remaining 68 patients in Olomouc. All patients were examined by CGH method in the cytogenetic laboratory at the Department of Hemato-Oncology, University Hospital Olomouc. Diagnosis of ALL was based on FAB and immunological classification. Clinical data are shown in Graphs 1, 2.

Methods

Conventional cytogenetics, FISH with locus specific, centromeric and painting probes (Vysis, Downers Grove, IL, USA; Cambio Ltd, Cambridge UK, Dako A/S, Glostrup, Denmark), M-FISH, Mband FISH (MetaSystems GmbH, Altlussheim, Germany) and CGH (Vysis Ltd, Cambridge UK, Dako A/S, Glostrup, Denmark), M-FISH, and painting probes (Vysis) were used for the determination of chromosomal imbalances.

Results

Unbalanced chromosomal changes were detected using CGH method in 87 (72.5 %) patients. The total number of 318 gains (46 gains of whole chromosomes and 50 chromosomal regions) and 334 losses were detected. The most frequent gains involved chromosomes 4, 4, 6, 9, 10, 14, 17 and X; losses were most frequently observed in chromosomes 9p, 12p, 13q, 14q, 15, 16, 22, X and Y (Fig. 1).

Conclusions

1. Employment of CGH in addition to CC and FISH in the examination of 120 childhood ALL patients revealed chromosomal changes in 115 (96 %) patients. (Graph 3)

2. Using CGH we confirmed that gains are mainly connected with whole chromosomes, while losses with chromosomal regions. The most frequent chromosome gained was chromosome 21 (40 patients), the most frequent region lost was 9p (19 patients) (Fig. 1).

3. CGH completed the conventional cytogenetics in 76 patients:
   - in 16 patients with unsuccessful cytogenetics (Fig. 2A, B, Graph 4)
   - in 20 patients with partial cytogenetic results (Graph 6)
   - in 40 patients with new additional changes found (Graphs 4, 5)

4. CGH did not confirm hyperdiploid or hypodiploid clones detected by cytogenetics or FISH in 16 patients due to low presence of these clones.

5. Detailed analysis of the 68 patients examined in the cytogenetic laboratory in Olomouc revealed the necessity of employing CGH method especially in patients with complex karyotype (Fig. 3, 4).

The results obtained in the present CGH study in 120 pediatric patients confirmed the findings of our first study in 65 childhood ALL patients, published in The Cancer Genetics and Cytogenetics, 123, pp. 114-122, 2000.

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