CYTOGENETIC FINDINGS OF PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA IN NATIONAL CHILDREN'S HOSPITAL FROM JANUARY, 2017 TO JUNE, 2018

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ABSTRACT

Acute Lymphocytic leukemia (ALL) is the most common cancer in children. Cytogenetics analysis plays an important role in classification and prognosis in ALL patients. ***Objective****s: to define the frequency of chromosomal abnormalities of ALL patients in children.* ***Methods****: 139 patients were diagnosed with ALL at National Children's Hospital- Hanoi- Vietnam from January/2107 to June/2018. Karyotype analysis and Fluorescence hybridization (FISH) techniques were applied to detect chromosomal abnormalities.* ***Results****: The proportion of male children is higher than that of females, at the age group of 1-10 years, accounting for 86.33%. Immune type predominant group prescursor B (preB) accounted for 92.09%. The frequency of cytogenetic abnormalities, including numerical and/or structural changes, was 36.70%.* ***Conclusion****: Normal karyotype was more frequent in our study. The frequencies of some cytogenetic abnormalities such as t(9;22), t(1;19), MLL- rearranged in our study were comparable to those reported in the literature.*

I. INTRODUCTION

Acute leukemia is a clonal expansion of white blood cell precursors in the blood, bone marrow, and various extramedullary tissues. The diagnosis of acute leukemia is based on the presence of more than 20% blasts in the peripheral blood or bone marrow. Acute Lymphoblastic Leukemia (ALL) is the most common childhood malignancy, accounting for close to 25% of all cancers in children and 72% of all cases of pediatric leukemia [1]. ALL occurs at an annual rate of 3 to 4 cases per 100.000 children lower than 15 years of age [2]. Approximately 3.000 children in the United States and 5.000 children in Europe are diagnosed with ALL each year [3].In the National Children's Hospital, Hanoi, Vietnam, there are 80 -100 new cases diagnosed with ALL each year, most of which are B-lineage ALL (B-ALL).

The World Health Organization (WHO) classification of B-ALL identifies 7 subtypes with recurrent genetic abnormalities: t(9;22)(q34;q11.2), BCR-ABL1; t(v;11q23), MLL rearranged; t(12;21)(p13;q22), ETV6-RUNX1; hyperdiploidy; hypodiploidy; t(5;14)(q31;q32), IL3-IGH; and t(1;19)(q23;p13.3), TCF3-PBX1 [4]. Although several specific recurrent chromosome aberrations and gene mutations also occur in T-lineage ALL(T-ALL), at present they are not used to delineate separate entities within T-ALL [5].

II. MATERIALS METHODS

From January 2017 to June 2018, we reviewed all cases with a final diagnosis of ALL including 130 cases of B-cell type and 9 cases of T-cell type. Definite diagnosis in all the cases was established

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based on morphology, cytochemistry, immunohistochemistry, and flow cytometric analysis in our center.

Cytogenetic findings by karyotype analysis from bone marrow to detect the abnormal chromosomes and Fluorescence In Situ hybridization (FISH) to detect the most common fusion oncogenes such as BCR-ABL, MLL-rearranged, ETV6-RUNX1 and TCF3-PBX1.

In this cross-sectional, descriptive study, we reported descriptive statistics, using the SPSS software package (version 16).

III. RESULTS

We conducted a cytogenetic analysis of 139 ALL patients, comprising 130 B-ALL and 9 T-ALL cases. The 139 ALL patients were composed of 53 females and 86 males, range: 6 months to 16 years. 83 (59.71%) cases at a mean age from 1 to 5; 37 (26.62%) cases at a mean age from 5 to 10; 13 cases at a mean age from 10 to 15; 5 cases lower than 1 year and 1 case older than 15 years.

Table 1: Immunophenotype

Immunophenotype		n	%
B-lineage	Pre B	128	92.09%
	Mature B	2	1.44%
T-lineage		9	6.47%
Total		139	100%

Karyotyping was unsuccessful in 45 (32.37%) patients: all specimens were cultured but did not have metaphases or had too few metaphases to be adequate or had too poor quality to be interpreted. There were 86 cases of successful cytogenetic analysis of B-ALL patients, with 61 (70.93%) cases showing normal karyotype. Normal karyotype were found in 4 out of the 8 (50%) T-ALL patients. The frequency of cytogenetic abnormalities, including numerical and/or structural changes, was 29.07% and 50% in the B-ALL and T-ALL patients, respectively and in 30.85% in total ALL.

Table 2: Distribution of karyotypes of ALL patients

Immunophenotype / Abnormalities	B-ALL (Pre B)	B-ALL (Mature B)	T-ALL	n (%)
Structure	**10**	0	**4**	**14/94 (14.89%)**
Hyperdiploid	**12**	0	0	**12/94 (12.77%)**
Hypodiploid	**3**	0	0	**3/94 (3.19%)**
Number and structure	**4**	0	0	**4/94 (4.26%)**
Complex (>4 changes)	**1**	0	0	**1/94 (1.06%)**
Total	**25/84**	**0/2**	**4/8**	**29/94 (30.85%)**

Table 3: Fluorescence in situ Hibridization

Translocation	Yes (%)	No	Other (%)	Number
BCR/ABL	**2/55 (3,64%)**	53	**3**	55
MLL- rearranged	**1/56(1,79%)**	55	**2**	56
ETV6/RUNX1	**3/27(11,11%)**	24	**8**	27
TCF3/PBX1	**1/30(3,33%)**	29	**2**	30
Total	**7**	161	**15**	168

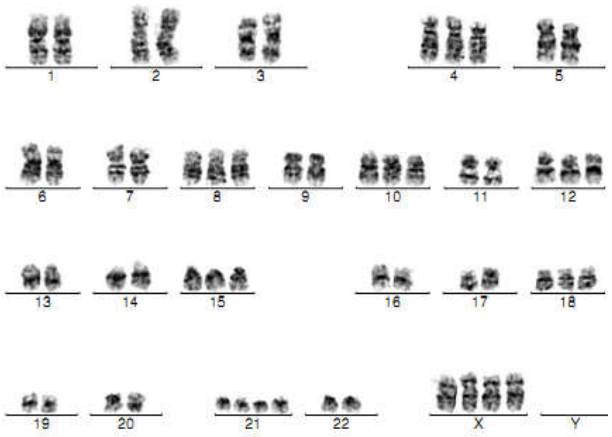

Figure 1: Hyperdipliod (BM170508)

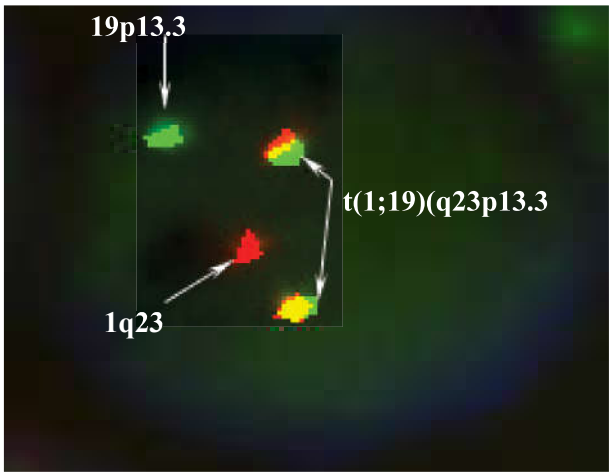

Figure 2: t(1;19)(q23;p13.3)-TCF3/PBX1

IV. DISCUSSION

Cytogenetic abnormalities in chromosomal number and structure are common in pediatric ALL and some have prognostic significance. These characteristics may contribute to the better outcomes observed in patients with hyperdiploid lymphoblasts. A number of recurrent chromosomal abnormalities have been shown to have prognostic significance, especially in B-pre cursor ALL. Some chromosomal abnormalities are associated with more favorable outcomes, such as high hyperdiploidy (51–65 chromosomes) and the ETV6–RUNX1 fusion. Others are associated with a poorer prognosis, including the Philadelphia chromosome t(9; 22), rearrangements of the MLL gene (chromosome 11q23), t(1;19) and hypodiploid lymphoblast.

In this study, we present cytogenetic findings on 139 pediatric ALL patients in our hospital and compare our findings with the relevant reports in the literature. We had a successful cell culture rate of 67,63%, which is comparable to that in the studies by Pullarkat and some one who had successful cell culture rates of 70 to 75% [7]. Unsuccessful cell cultures may be due to the nature of malignant cells as well as technical and quality of sample.

We detected 30,85% of ALL with chromosome abnormalities by using karyotype analysis, including 14,89% tructural abnormally and 15.96% numerical abnormally. There were 4 cases with abnormal chromosomes both in number and structure, one of them had a complex karyotype with 4 chromosomal changes, belonging to very poor prognosis group [8].

Using advanced methods in cytogenetics as FISH we found the frequency of t(9;2), MLL- rearranged and t(1;19) were 3.64%; 1.79% and 3.33% respectively. Thus, our results are in the same range as those reported previously. We found a lower incidence of t(12;21) (11.11%) than the other published

studies in the pediatric age group [9]. FISH also detected other abnormalities in the number of genes that belonged to translocations.

So due to the use of the conventional G-banding technique and FISH we detected 36.70% of our ALL patients with abnormal karyotypes. FISH were used to examnine abnormal chromosomes in patients who have failed to perform routine karyotype and small changed chromosomes .

5. CONCLUSION

Cytogenetic analysis in ALL plays an important role in the classification and prognosis of the patients. In our study the frequency of detection of abnormal chromosomes is lower than the other studies but the. The frequencies of some cytogenetic abnormalities such as t(9;22), t(1;19), MLL- rearranged that detected by using FISH technique in our study were comparable to those reported in the literature.

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