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Original Research Article

CHROMOSOMAL TRANSLOCATIONS IN ACUTE LYMPHOBLASTIC LEUKEMIA IN NORTH INDIAN POPULATION

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ABSTRACT

Introduction: Recurrent chromosomal abnormalities in the malignant cells of patients with acute leukemia are hallmark of the disease. Specific aberrations, which are frequently indicative of consistent underlying molecular lesions, can assist or even establish the diagnosis and determine optimal therapy.

Materials and methods: Karyograms of 51 North Indian patients (44 males and 7 females) of acute lymphoblastic leukemia (ALL) from the age group of 2 to 42 years were prepared and observed for the various chromosomal translocations and their frequency.

Results: Out of total thirty nine analyzed cases, translocation was detected in thirteen cases (33.33%), most frequent chromosomal translocation was t (9;22) being detected in 4 cases (10.25 %), t (4;11) in three cases (7.69%) and one case (2.56%) each was found with t (8;21), t (1;3), t (8;14), t (1;8), t (1;19), t (4;12), t (3;19). There was random distribution of various chromosomal translocations in different age group and sex.

Conclusion: The unique finding of the present study was reporting of t (8;21), t (1;8), t (4;12) and t (3;19), each with one case which was not observed previously by any author in acute lymphoblastic leukemia in North Indians. The findings of the present study may be useful for pediatricians and physicians in predicting outcome, remission, survival and treatment response in acute lymphoblastic leukemia (ALL).

KEY WORDS: Acute lymphoblastic leukemia, p-arm, q-arm,Translocation.

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INTRODUCTION

Recurrent chromosomal abnormalities in the malignant cells of patients with acute leukemia are hallmark of the disease [1]. Chromosomal aberrations that are important events in leukemogenesis are widely used in diagnosis and risk stratification. In childhood acute lymphoblastic leukemia (ALL), numerous good and high-risk cytogenetic subgroups have been identified which are regularly used to stratify patients to particular therapies [2]. A significant number of patients are not cured despite intensive treatment. At the same time, some highly curable patients are treated too intensively and suffer from unnecessary side effects of the chemo- and radiotherapy applied. In order to further improve the therapeutic results the initial karyotype proved to be one of the most

reliable prognostic parameters, leading to the suggestion of developing genotype-specific therapies [3]. Present study was done to analyze various chromosomal anomalies in North Indian population.

MATERIALS AND METHODS

The present study was descriptive type. Patients were screened in the Department of Pediatrics and the sample was collected from the Department of Pathology. Bone marrow and peripheral blood of diagnosed cases of ALL was taken with their consent. Culture of bone marrow and blood sample were done; a trypsin-Giemsa technique was used for chromosome banding. Karyogram was prepared and 20- 25 metaphases were analyzed in each case for various chromosomal anomalies in the Cytogenetic Laboratory of the Department of Anatomy, King George's Medical University, UP, Lucknow, India.

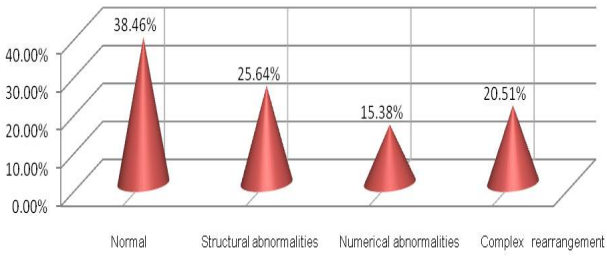
OBSERVATIONS AND RESULTS

This study was conducted during the period from April 2012 to August 2013 and includes 51 patients (44 males and 7 females) of age group 2 years to 42 years. Out of fifty one ALL patients, only thirty nine cases (76.47%) could provide good chromosomal spread and karyogram was obtained. Amongst thirty nine successful cases, twenty four exhibited abnormal karyogram and fifteen cases showed normal karyogram. Both numerical and structural chromosomal aberrations were observed. As these abnormalities occurred in combination in many cases, their karyotype appeared complex. Of total thirty nine cases, structural chromosomal abnormalities were observed in ten cases (25.64%) and numerical chromosomal abnormalities were noted in six cases (15.38) while eight cases (20.51) showed complex karyogram (Table1, Fig.1).

Table 1: Distribution of different types of karyogram in analyzed cases.

Karyogram	Normal	Structural chromosomal abnormalities	Numerical chromosomal abnormalities	Complex rearrangement
No. of cases (n=39)	15	10	6	8
Percentage (%)	38.46%	25.64%	15.38%	20.51%

Fig. 1: Bar Diagram showing distribution of various types of chromosomal abnormalities.

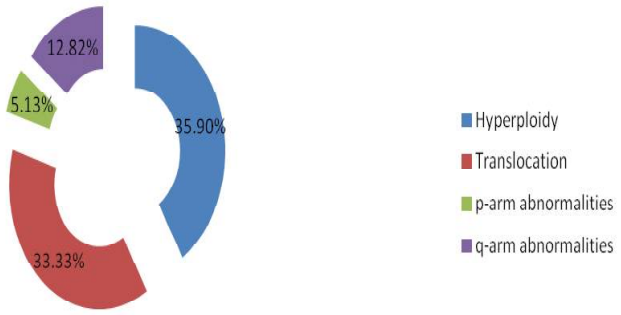


Out of total thirty nine analyzed cases, translocation was detected in thirteen cases (33.33%), p-arm abnormality (partial deletion) was present in two cases (5.13%) and q-arm abnormality (partial deletion) was present in five cases (12.82%); one case showed partial deletion of q arm of chromosome 5 and 11 both and in 14 cases (35.90%) hyperploidy was present (Table 2, Fig. 2).

Table 2: Percentage of different types of chromosomal abnormalities in analyzed karyogram.

Type of Aberration	Number of cases (n=39)	% out of total analyzed cases
Hyperploidy (>50 chromosome)	14	35.90%
Translocation	13	33.33%
p-arm abnormality (partial deletion)	2	5.13%
q-arm abnormality (partial deletion)	5	12.82%

Fig. 2: Incidence of various chromosomal aberrations.



The most frequent chromosomal translocation was t (9;22) being detected in 4 cases (10.26 %), t (4;11) in three cases (7.69%) and one case (2.56%) each was found with t (8;21), t (1;3), t (8;14), t (1;8), t (1;19), t (4;12), t (3;19) (Table 3, Fig. 3-6)).

Table 3: Various structural anomalies and their distribution in analyzed cases.

S.No.	Structural chromosomal abnormalities	Number of patients	% out of total karyogram obtained cases (n=39)	% out of total abnormal cases (n=24)
1	t (9;22)	4	10.26%	16.67%
2	t (4;11)	3	7.69%	12.50%
3	t (8;21)	1	2.56%	4.17%
4	t (1;3)	1	2.56%	4.17%
5	t (8;14)	1	2.56%	4.17%
6	t (1;8)	1	2.56%	4.17%
7	t (1;19)	1	2.56%	4.17%
8	t (4;12)	1	2.56%	4.17%
9	t (3;19)	1	2.56%	4.17%

Fig. 3: Karyogram - 47XY, +21, t(4;12), t(9;22)

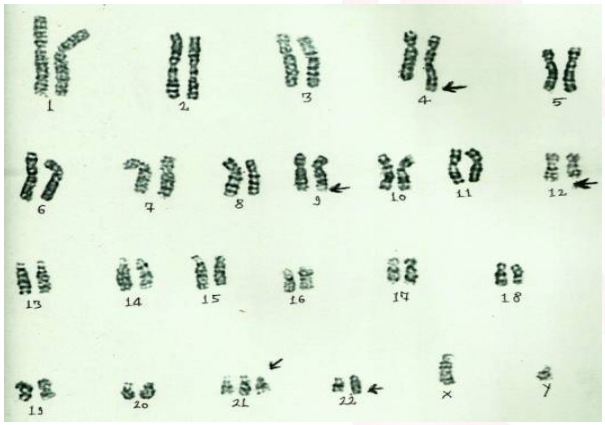


Fig. 4: Karyogram-46XY, t(1;8)

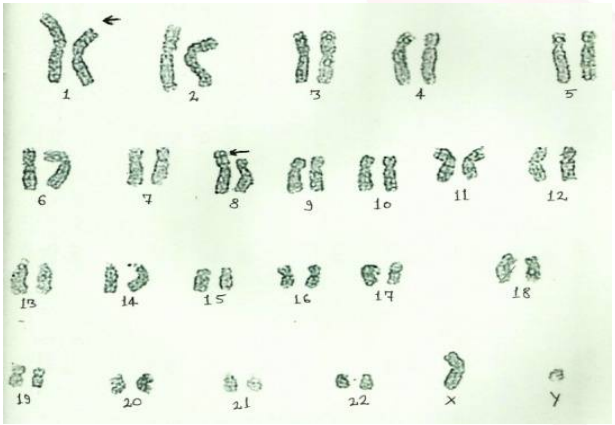


Fig. 5: Karyogram-47XY, +13, t(3;19)

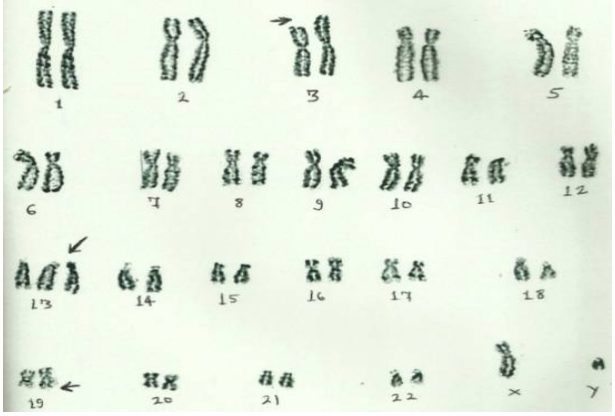
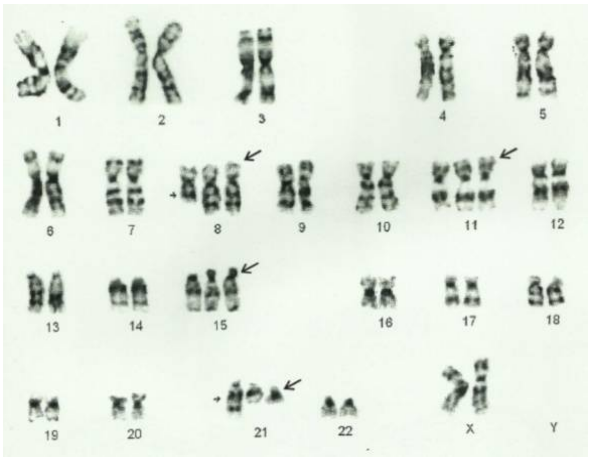


Fig. 6: Karyogram-50XX, +8, +11, +15, +21, t(8;21)



DISCUSSION

Conventional cytogenetic has long been regarded as the gold standard for chromosome analysis in leukaemia, despite the advent of molecular cytogenetics. Some of the previous studies have also recognized the correlation between cytogenetic findings and some clinical and hematological features as well as the stage of leukemic cell maturation. This contributes significantly in designing the potential therapeutic strategy. In the present descriptive study, we analyzed the cytogenetic features of 51 patients (44 males and 7 females) from age group 2 to 42 years with Acute Lymphoblastic Leukemia. Structural chromosomal abnormalities were documented in 10.97% of ALL patients in Caucasian population [4]. In our study on North Indian population, we found 25.64% (10 cases) with structural chromosomal abnormalities. On comparing with previous studies, we found that percentages of structural abnormalities were different in different populations; it may be due to difference in their environmental factors which causes chromosomal abnormalities in ALL.

Out of total 39 analyzed cases, present study showed translocation in 33.33% (13 cases) which runs parallel with the findings of Jena et al (2002) who found 31.8% cases of translocation in his study on South Indian population [5]. Chromosomal translocations ultimately result in the de-regulation of key cellular proteins, especially those coded by proto-oncogenes and tumor suppressor genes, which are critical functional regulators of the cell [6].

In the present study on North Indian population,

most frequent chromosomal translocation was t (9; 22) being detected in 4 cases (10.26 %), which is very much similar to a study conducted on Chinese population by Tien et al (1992) who reported this translocation in 12.5% cases [7] and on Hispanic patients in 11.29% cases [8]. The Philadelphia chromosome t (9; 22) leads to production of a BCR-ABL1 fusion protein with tyrosine kinase activity. Inhibitors of the BCR-ABL tyrosine kinase, such as imatinib mesylate, are effective in patients with Ph+ ALL. We found t (4;11) in 7.69% (3 cases) which was previously documented in, 6.8% cases of ALL in South Indian population [5]. t (4;11) was also documented in past by many authors [4,9-11]. Both infants and adults with t (4;11) translocation are at high risk of treatment failure, children with t(4;11) translocation appear to have a better outcome than either infants or adults [12]. We observed t (1;3) in 2.56% (1 case) which runs parallel with the findings of Okaly et al (2012) who observed it in 3% cases in Indian patients [10]. Bloomfield et al (1981) also reported t (1;3) in his study [11]. In our study , t (8;14) was present in only 2.56% (1 case),which was previously reported in 6.45% cases of Japanese population [13] and 7.14% cases of Indian population [10]. t (1;19) contributes 2.56% (one case) of total karyogram in the present study. t (1;19) was also reported in past in Japanese [13], Chinese [7], and in Indian population [10]. t (1;19) translocation had been associated with inferior outcome in the context of antimetabolite-based therapy [14]. t (8;21), t (1;8), t (4;12), and t (3;19) were observed in the present study, each with one case which was not reported previously by any author in acute lymphoblastic leukemia. This type of translocations could not be compared as very few citations have been encountered in North Indian Population.

Further investigations are required to confirm the findings of present study because in ALL chromosomes exhibits poor morphology, spread poorly and appear blurred and fuzzy with indistinct margins, making banding studies challenging.

CONCLUSION

The unique finding of the present study was reporting of t (8;21),t (1;8), t (4;12), and t (3;19), each with one case which was not observed previously by any author in acute lymphoblastic leukemia in North Indians. The findings of the present study may be useful for the pediatricians and physicians in predicting outcome, remission, survival and treatment response in acute lymphoblastic leukemia.

Conflicts of Interests: **None**

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