Original Research Article

A comprehensive study on the cytogenetic and hematological parameters in different phases of chronic myeloid leukemia

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Abstract

Background: Chronic myeloid leukemia is a tri-phasic disorder of myeloid lineage of hematopoietic system, naturally exhibiting a chronic stage, followed by an ill-defined accelerated phase and terminal blastic phase and characterized by presence of t(9;22). **Objective:** The objective of the study was to determine phase wise distribution of cytogenetic and hematological parameters in known cases of CML. **Materials and Methods:** Previously diagnosed cases of CML were included in this analytical study. Karyotyping was done for cytogentic analysis along with hematological examination. **Results:** The study was conducted on 52 cases of CML. Out of these, 42 cases showed t(9;22) and 7 cases showed t(9;22) along with other chromosomal aberrations on karyotyping. Chronic phase CML cases were 40, while accelerated and blastic were 5 and 4 respectively. The analysis of hematological workup revealed the highest value of mean Hb count and the mean platelet count in the accelerated phase of CML. While the mean values of blast count, basophil count and TLC increased progressively as disease progressed from chronic to blastic phase. **Conclusion:** The t(9;22) may be the initial presentation in CML as seen in majority of chronic phase patients, the additional chromosomal aberrations are seen more frequently in accelerated and blastic phases and are responsible for the progression of disease. Similar pattern of stage wise deterioration was observed for the hematological parameters.

Key Words: CML, Phase, Cytogenetics, Hematological parameters.

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INTRODUCTION

Clinically CML progresses through three distinct phases: A chronic phase that is easily controlled, followed by an ill-defined unstable accelerated phase, leading to a terminal blastic phase. The blastic phase resembles acute leukemia and is highly refractory to chemotherapy with ≤20% response rate and a median survival of 3–6 months.[1] Although the presence of t(9;22) also known as Philadelphia chromosome may be the initial event in CML, the acquired additional cytogenetic abnormalities are responsible for progression of disease to more aggressive phase.[2] The objective of the study is to find out the chromosomal and hematological parameters associated with the different phases of CML and thus explore their role in the pathogenesis and evolution of the disease.

MATERIALS AND METHODS

It is an analytical cytogenetic study of 52 cases of CML where karyotyping was done on bone marrow samples and peripheral blood samples. The marrow aspirate and blood specimens were incubated in RPMI 1640 culture media for 72 hours. Colcemid solution was added and centrifugation was done. The sample was again incubated for ½ hour after adding hypotonic saline solution. Cell

button obtained was suspended in methanol + acetic acid suspension. Slides were prepared and treated with trypsin. Finally, Giemsa stained slides were microscopically assessed and karyotyping was done by cytovision software and also by manual method. The hematological analysis involving complete blood count –i.e; haemoglobin estimation, total and differential leukocyte counts and platelet count was done simultaneously for all the cases.

RESULTS

52 cases of CML were included in this study conducted in a tertiary care hospital in north India. The study was conducted over a period of one year wherein 43 cases were in chronic phase, 5 cases were in accelerated phase and 4 were in blastic phase of CML at the time of presentation. Chronic myeloid leukemia is classically associated with the presence of aberration, the most consistent being translocation t(9;22). A total 49 out of 52 cases showed t(9;22) while 3 cases in chronic phase showed normal karyogram. (Table 1) Frequency of chromosomal aberration other than t(9;22) also known as "additional chromosomal aberrations" increased as the CML progressed from chronic phase (6.97%), to accelerated phase (40%) and then to blastic phase (50%). (Table 2) The hematological parameters also correlated with phases of CML. The mean value of hemoglobin and platelets count was highest in accelerated phase that is 8.3±0.74 gm/dl and 482002±56778/cu.mm. respectively. Total leukocyte count, Blast cell count and Basophils count increased as disease progressed from chronic to blastic phase. (Table 3).

Table 1: Phase wise incidence of Disease and t(9;22) positivity

	Phase-wise incidence of CML		t(9;22) present in different phases of CML			
Phase of CML	Number	%	Present	%	Absent	%
Chronic	43	82.69	40	93	3	7
Accelerated	05	9.62	05	100	0	0
Blast	04	7.69	04	100	0	0
Total	**52**	**100**	**49**		**3**	

Table 2: Phase wise association of additional aberrations

	Additional chromosomal aberrations			
Phase of CML	Present	%	Absent	%
Chronic	3	6.97	40	93.03
Accelerated	2	40.0	3	60.0
Blast	2	50.0	2	50.0

Table 3: Association of hematological parameters with phases of CML

Hematological Parameters (Mean value ± SD)	Phases of CML		
	Chronic	Accelerated	Blastic
Hemoglobin (gm/dl)	7.61±1.66	8.30±0.74	7.25±0.93
Total Leukocyte count (/cu.mm.)	80251±64672	126434±73358	131250±78292
Blast cell (%)	4.69±5.61	11±2.28	30±4.74
Basophils (%)	6.37±1.47	24.8±3.54	22.25±3.34
Platelets (/cu.mm.)	581080±213499	482002±56778	697500±156104

DISCUSSION

Chronic myeloid leukemia is very common malignancy of blood cells involving myeloid lineage. We observed that most of the patients were in chronic phase of CML (82.69%) followed by accelerated phase (9.62%) and blastic phase (7.69%). Almost all the studies done previously showed similar results.[3,4] 40 out of 43 cases in chronic phase showed positivity for t(9;22) (i.e, 93%) while all the cases in accelerated and blastic phase had t(9;22) (100%). While additional chromosomal abnormality was present in 3 out of 43 cases of chronic phase CML (6.97%) 2 out of 5 (40%) and 2 out of 4 (50%) in cases of accelerated and blastic phase of CML respectively. Statistically, association between phase and presence of additional aberrations was significant (p=0.010). Additional chromosomal abnormalities in Ph+ve cells may appear in approximately 5% of patients with newly diagnosed CML in chronic phase, according to several studies.[5,6] Other studies also found higher frequencies of additional chromosomal abnormalities as the CML progressed to accelerated and blastic phase similar to present study. [7, 8] Most of the hematological parameters were in accordance with phases of CML. Blast cell counts (4.69±5.61, 11±2.28, 30±4.74) and total leukocyte counts (80251±64672, 126434±73358, 131250±78292) increased from chronic to blastic phase. Hemoglobin count reflected anemic picture in all the phases and was lowest in blastic phase. Basophils count

showed increased values in accelerated and blastic phase compared to chronic phase. Thrombocytosis was present in all the three phases with highest values in blastic phase. These findings were similar to other studies done previously. [9, 10]

CONCLUSION

The cytogenetic and hematological markers of CML are important tools used for diagnosis, clinical staging, prognosis and treatment management of the disease. As such complete laboratory workup including hematological and cytogenetic evaluation of each CML patient becomes mandatory at the time initial diagnosis as well as during treatment and follow up.

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