Prevalence of 7q deletion in patients with Acute myeloid leukemia .

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ABSTRACT

Introduction: Deletion of critical regions on long arm of chromosome 7 is important in pathogenesis of acute myeloid leukemia (AML). These regions include 7q22 and 7q31 which carry certain tumor suppressor genes which if deleted can result in uncontrolled division of myeloid cells.

Aims: To estimate prevalence of 7q deletion in patients with acute myeloid leukemia (AML).

Materials and methods: Retrospective study was done on 25 bone marrow samples diagnosed with Acute myeloid leukemia referred to Division of Human Genetics St.John's Medical college, Bangalore. Samples were subjected to standard protocol for karyotyping and FISH. Percentage of patients who were positive for 7q deletion was calculated.

Results: Out of 25 samples, 5 samples were positive for 7 q deletion accounting to 20% of total patients diagnosed with AML.

Conclusion: Presence of 7q deletion can be a poor prognostic marker since tumour suppressor genes are present in these regions. Hence cytogenetic markers are very important in deciding treatment and prognosis in these patients.

Keywords: 7q deletion, Acute Myeloid leukemia ,FISH, Karyotyping

INTRODUCTION

Chromosomal abnormalities are of prognostic significance in leukemias. Acute myeloid leukemia(AML) is characterized by wide variety of chromosomal abnormalities that will help in classification, diagnosis, treatment and prognosis in these patients. Most common chromosomal abnormalities in AML include t(8;21),t(15;17), inv(16), chromosome 7 and 11 abnormalities. Chromosomal translocations, such as t(8;21), t(15;17), t(16;16) or inv16 are usual in younger patients whereas deletion of chromosome 5 is more prevalent in patients older than 60 years who are likely to present as myelodysplastic syndrome(MDS)[1].This can be diagnosed by conventional karyotyping or molecular cytogenetic techniques like Flourescence in situ Hybridisation (FISH). The long arm of human chromosome 7 between 7q22 and 7q36 has been identified as a region harboring one or more tumor-suppressor genes (TSGs) inactivated in acute myeloid leukemia (AML).Hence deletion or mutation of these genes is likely to have poor prognosis and high chance of relapse in these patients. Aim of present study was to estimate prevalence of 7q deletion in patients with AML.

MATERIALS AND METHODS:

Ethical clearance was obtained from Institutional Ethical Committee. Informed consent taken from patient or his /her relatives before test. Patient age group ranged 1-60 yrs(Both males &females).A retrospective study was carried on 25 Bone marrow samples of patients diagnosed with acute myeloid leukemia was referred to Division of Human Genetics, Department of Anatomy, St.John's Medical college ,Bangalore from October 2019 to March 2020 for a period of six months. Percentage of patients showing positive results were calculated.

Bone marrow samples were subjected to standard unstimulated lymphocyte culture. Incubation was done for overnight and 24 hours followed by harvesting and fixation on slide.GTG banding was done also standard Protocol for FISH with overnight hybridisation of commercially available deletion 7q probes from Metasystems was used. Slides were observed under florescent microscope. Analysis was done by automated karyotyping system. Around 200 cells were analysed .Probe specification included the 7q22 probe, labelled in red, covers a 396kb region including the telomeric end of the RELN gene and extending beyond the marker D7S658 and the 7q31 probe, labelled in green, covers a 203kb region including the TES gene (Figure 1) .Deletion of these regions were documented.(Figure 2,3,4)

RESULTS:

Presence of 7q deletion is an unbalanced chromosomal abnormality accounting to 20% of total cases in present study (Table 1).

Table 1: Prevalence of 7 q deletion in patients with AML

	POSITIVE	NEGATIVE	PERCENTAGE
Sample size(n=25)	5	20	20%

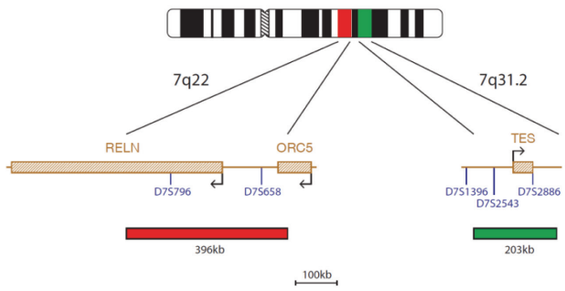

Figure 1: Critical regions involved in AML on chromosome 7q

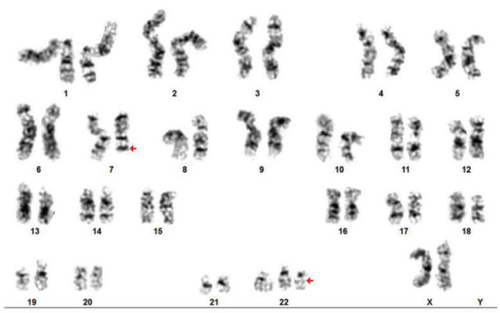

Figure 2: Karyotype showing deletion of critical regions on chromosome 7q

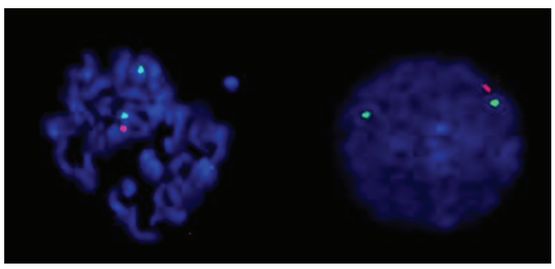

Figure 3 : Metaphase and interphase cell in FISH showing deletion of 7q22 region in red

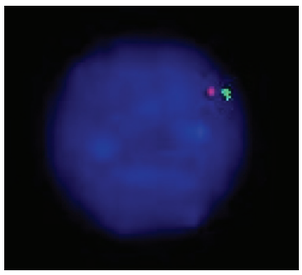

Figure 4: Interphase cell showing deletion of both 7q22(red) and 7q31(green) critical regions

DISCUSSION:

Presence of 7q deletion is an unbalanced chromosomal abnormality accounting to 20% of total cases in present study. In myeloid disorders involving -7/del (7q) signaling pathways involving RAS proteins are affected. There are two commonly deleted regions (CDR): one at 7q22, the other at 7q31-34. RELN (7q22) encodes a large secreted protein related to extracellular matrix proteins, a family of proteins that contains multiple epidermal growth factor (EGF)-like proteins.

Marchesi F et al did concise review on chromosomal abnormalities in adult non promyelocytic keukemia concluded that Monosomy 7 and deletion of 7q are present as a single chromosomal alteration only in 35% and 33%, respectively, of all AML case.

In a review done by LH Shi et al., AML patients with chromosome 7 aberrations are characterized by frequent multi-lineage dysplasia in bone marrow cells and poor clinical course with a low rate of clinical response (20-30%)[1].

In a cytogenetic study done by Heba N. Abdelrazik et al., out of 20 AML patients two had 7q deletion accounting to 10% of total cases. After following up patients for one year of treatment, they concluded that patients who had normal FISH results showed a higher percentage of complete remission while patients with monosomy or deletion had higher rates of death or showed no response to therapy[3].

In a FISH study done by Mohammed Amr et al, out of 29 patients with AML 6 had 7q deletion accounting to 21% of total cases .They concluded that patients with del(7q) were found to have better outcome than cases with monosomy 7 in adult AML and MDS patients[4].

Michael Wang et al., who did study on AML patients came to a conclusion that patients with monosomy 7 or 7q deletion had poor response to chemotherapy and might require a hematopoietic stem cell transplantation[5].Molecular mapping done by Hong Liung et al., on chromosome 7q deletion showed allelic loss in three distinct loci D7S486 , D7S2456 and D7S677 [6].

Poire et al., who did two year study on 1109 patients with AML, concluded that Stem cell transplantation in -7/7q- AML provides durable responses in one third of the patients. The presence of -7/7q- with or without complex karyotype in , abn(17p) or inv(3) is associated with a better survival after Stem cell transplantation. On the contrary, addition of monosomal karyotype, -5/5q-, abn(17p) or inv(3) identifies a sub-group of patients with poor prognosis even after SCT [7].

In a retrospective study done by Henrik Hasle et al., out of 258 patients with AML , del(7q) was present in 21 patients and del(7q) with other chromosomal abnormalities was present in 65 patients. They concluded that cytogenetic aberrations considered favorable in AML t(8;21), inv(16), t(15;17), t(9;11) were strongly associated with del(7q) and a higher 5-year survival rate[8].

Hence conventional karyotyping and FISH are powerful tool in treatment, outcome and prognosis in patients with AML. They also play a key role in risk stratification in these patients.

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Conflicts of interest :none

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