Trisomy 6 as Sole Cytogenetic Abnormality in Acute Myeloid Leukemia “A Case Series”

Salil Vaniawala, Avani Kathiriya, Pankaj Gadhia

Molecular Cytogenetic Unit, S. N. Gene Laboratory and Research Centre, Surat, India

Corresponding author email: pankakigadhia@gmail.com

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Abstract Cytogenetic analysis is a key component in diagnostic of Acute Myeloid Leukemia (AML). The malignant cells in most patients with AML have non-random, acquired chromosomal abnormalities. Here in we report 03 cases of trisomy 6 as sole abnormality in AML. The study includes two males and a female having age between 37 to 52 years.

Routine short term bone-marrow cultures followed by G-banding revealed two cases of AML-M1 and one case of AML-M2 as sole trisomy-6 abnormalities. As prognostic significance is not well established, more studies are required to assign the role of trisomy 6 in the development of leukemia.

Keywords Bone marrow; G-Banding; Karyotype; AML; Trisomy 6

Introduction

Acute myeloid leukemia (AML) is a cancer of the myeloid line of blood cells, characterized by the rapid growth of abnormal white blood cells. The single most important prognostic factor in AML is cytogenetics. It is well established that identification of cytogenetic abnormalities plays an important role in the diagnosis of leukemias. The common cytogenetic abnormalities are t (8;21), t (15;17) and inv (16) which considered being good prognosis. While +8, +21, +22, del (7q) and del (9q) chromosomal abnormalities consider as intermediate risk category (Heim and Mitelman, 1985; Mitelman, 1995).

The distribution of numerical changes is clearly non-random in leukemias. In approximately 7% of hematologic neoplasms with identifiable chromosomal abnormalities, the simple trisomic aberration is the only cytogenetic change observed (UKCCG, 1992).

Acute myeloid leukemia (AML) comprises a spectrum of hematologic malignancies with variable outcomes. A hallmark of AML is maturation arrest of myeloid cells, which accumulate in peripheral blood and bone-marrow. The most common trisomy 8 is strongly associated with myeloid disorders.

The trisomy 6 has been reported as the sole karyotypic aberrations in hemalogic disorders. This abnormality generally found with AML and reported with bone marrow neoplasia (Jonveaux et al., 1994; Mohamed et al., 1998). There seems to be an association between trisomy 6 and cytopenias, with marrow hypoplasia, and the abnormality is detected in preleukemic cases upon transformation to AML (McCullough et al., 2004). Trisomy 6 was reported as the sole chromosomal abnormality in aplastic anaemia as early as 1976. Subsequently ten reports were published describing 18 cases of AML presented with trisomy 6 as sole karyotypic abnormality (Yu et al., 2014). In the present study, we report three more cases of acute myeloid leukemia with trisomy 6 as sole cytogenetic abnormality.

Case reports

Case 1

A 37 year old female bone-marrow showed hyper cellular marrow with marked proliferation of tumor blast population (>55%). Bone-marrow also showed occasional megakaryocytes which were suggestive of AML-M1. Blood pictures showed haemoglobin (8 g/dL), WBC (15.60 × 10⁹/L) and platelets (10 × 10⁹/L).
10^9/L). Cytogenetic study of G-banded karyotype revealed 47,XX,+6[4]/46,XX[46] (Figure 1).

![Figure 1: G-banded karyotype showing 47,XX, +6 chromosome complements](image1)

**Case 2**

A 52 years old male showed hyper cellular bone-marrow with tumor blast population (78%). The blood profile showed 10.7 g/dL haemoglobin content, 26.75 X 10^9/L WBC and 21 X10^9/L platelets. G-banded karyotype showed 47,XY,+6[7]/46,XY[8] (Figure 2).

![Figure 2: G-banded karyotype showing 47,XY, +6 chromosome complements](image2)

**Case 3**

A 40 year male where bone-marrow report showed normal bone-marrow component replaced by blast cells (82%). The blood picture revealed haemoglobin content 12.5 g/dL, WBC count was 32 X 10^9/L and platelets were 32 X 10^9/L. The G-banded karyotype revealed 47,XY, +6[10]/46, XY[30] (Figure 3).

![Figure 3: G-banded karyotype showing 47,XY, +6 chromosome complements](image3)

**Discussion**

Numerical aberrations as the sole karyotypic anomalies, including single or multiple loses or gains are found in approximately 15% of all cytogenetically abnormal haematological neoplasms (Heim and Mitelman, 1986). The first case of sole trisomy 6 was reported in a patient with aplastic anaemia (AA) (Swerdlow et al., 2008). The other reports revealed that trisomy 6 was associated with hypoplastic bone marrow and AML prior to hypocellular bone marrow with MDS (Jonavaux et al., 1994; Yu et al., 2014). In addition, Starza et al. (1998) have also reported Trisomy 6 as hallmark of dysplastic in bone marrow aphasias.

Trisomy 6 as a sole chromosomal abnormality is relatively rare in the patients with AML, myodisplastic disorders and bone marrow hypoplasia and its prognostic significance in AML needs to be elucidated (Kelly et al., 2009). It is known that three out of four AML patients with + 6 in one series showed AML-M1 morphology and expression of stem cell antigen CD 34 on the leukemic blasts, suggesting that trisomy 6 may be associated with more primitive form of AML.

Acute myeloid leukemia (AML) comprises a spectrum of myeloid malignancies which are often associated with distinct chromosomal abnormalities which provide us with important information for prognosis of disease. In current study, retrospective database searched revealed a total of confirmed 436 cases of AML, of which, only 3 cases of sole trisomy 6 were noticed between year 2004 and 2014. There is some
controversy as to the prognostic impact of trisomy 6 as sole aberration in AML. It has been documented that +6 could be one of the factors for unfavourable prognosis (Jackson et al., 1990).

In the present study sole trisomy 6 was noticed with AML-M1 (two cases) and AML-M2 (one case) according to FAB criteria. It is interesting to note that Mohamed et al. (1998) reported that the increase in blasts has direct relation with an increase in proportion of trisomy 6 cells. Our results are in good agreement with above cited study which is very clear from case reports section. In conclusion, we suggest that trisomy 6 is a non-random clonal cytogenetic marker of myeloid disorders associated with cytogenetic and bone hypoplasia.

Ethical clearance: The ethical clearance was obtained from Institutional ethical committee.

Authors’ contribution
The work was carried out in collaboration. Author PG designed study, wrote protocol and prepared first draft of MS. Author SV performed culture and microscopic analysis and made preparation of karyotypes. AK managed the literature searches and analysis of data.

All authors read and approved the final MS.

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