Trisomy 9 in a Patient with Acute Myelogenous Leukaemia FAB Type M2: A Rare Occurrence

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Abstract Complete trisomy 9 is a rare cytogenetic abnormality in haematological malignancies. Here we present the case history of a patient with clinical diagnosis of acute myeloblastic leukaemia (FAB type M2) and having trisomy 9 with adverse outcome.

Keywords Trisomy 9 · Acute myeloid leukemia · Karyotype

Introduction

The association of trisomy of various chromosomes with haematological malignancies is well established. The presence of some single acquired autosomal trisomies supports the diagnosis and may be indicative of prognosis in these disorders [1]. Trisomy 8 is very common in acute myeloid leukemia (AML) and portends poor prognosis across all AML subgroups at all ages [2]. Trisomy 9 is rarely reported, when present has intermediate prognosis and has been considered a marker for benzene-related leukemogenesis [3, 4]. Both trisomy 8 and 9 are common in systemic mastocytosis and myeloproliferative disorders [5].

Here, we present a case of a 65-year-old lady with AML-M2 and rapidly downhill course in whom conven-

tional cytogenetic analysis revealed trisomy of chromosome 9. To the best of our knowledge this is an extremely unusual association.

Case Report

A 65-year-old woman belonging to a low socioeconomic stratum with a long history of tobacco smoking presented with progressively worsening high-grade fever, pallor, weakness, bone pains and fatigability over 5 months. On examination she was pale, icteric and had liver palpable 2 cm below the costal margin. A complete blood count showed haemoglobin 8 gm/dl, TLC $6.6 \times 10^3/\mu\text{l}$ and platelets $24 \times 10^3/\mu\text{l}$. Peripheral smear revealed 6% blasts, some with Auer rods. Neutrophils showed dysplastic features including hypogranularity, pseudo Pelger Huet forms and abnormal large granules. A bone marrow aspirate was hypercellular with 36% blasts that were positive for Sudan black and MPO and negative for NSE. Her clinical findings and results of investigations were consistent with a diagnosis of Acute Myeloid Leukaemia type 2. She was put on palliative care. Cytogenetic analysis of the patient's bone marrow cells was performed at the time of diagnosis of AML type 2. The chromosomes were G-banded and 35 metaphases were analysed which revealed an addition of chromosome 9, 47, XX + 9(90%) and 46, XX (10%). The chromosome spreads and interphase nuclei were examined from 24-h unstimulated bone marrow cells. They were Giemsa-Trypsin-Giemsa (GTG) banded and karyotypes were described according to ISCN 2005 [6]. The patient died because of multiple organ failure 6 months after the diagnosis. The patient presented here is one of the rare cases in which trisomy 9 is found in AML type2 and is the first report from India (Fig. 1).

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Fig. 1 Bone marrow Karyotype of the patient in December 2007. 47, XX + 9 chromosomal complement

Discussion

Diagnostic cytogenetics is widely recognized as one of the most important prognostic determinants in AML [2]. Complex karyotype $-7/7q^-$ and (17q) is associated with a poor prognosis; a normal karyotype, loss of Y chromosome, deletion 11q, deletion 12p and deletion 20q as single alterations with a good prognosis. Aberrations like rearrangements of 3q21q26, trisomy 8, trisomy 9, translocations of 11q and del (17p) [3] is associated with intermediate prognosis. Although the presence of a clonal chromosome abnormality in bone marrow is usually indicative of haematological malignancy, not all apparent chromosome abnormalities can be taken as proof of malignancy. Trisomy 9 is a relatively rare chromosomal abnormality, associated with specific patterns of multisystem dysmorphism and a wide spectrum of congenital anomalies [7]. There are few reports in the literature where trisomy 9 is diagnosed prenatally [7–10]. Mark HF and his colleagues in 1999 were the first ones to report a case of secondary AML with trisomy 9 using FISH technique [11]. We present a report of a patient showing trisomy 9 in adult female patient who evolved AML and died in a very short time period. This report shows that trisomy 9 is not only an extremely rare phenomenon in AML but may have also contributed to a particularly poor outcome in this patient. Thus, this report clearly demonstrates the importance of cytogenetics in the routine diagnosis and treatment of leukemic patients. Hence, diagnostic

cytogenetics should be considered as a part of the routine work up of patients with AML at diagnosis with a view to provide the framework for a specific treatment approach.

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References

1. United Kingdom Cancer Cytogenetics Group (UKCCG) (1992) Primary, single autosomal trisomies associated with haematological disorders. *Leukemia Res* 16:841–851
2. Grimwade D, Walker H, Oliver F et al (1998) The importance of diagnostic cytogenetics on outcome in AML: analysis of 1,612 patients entered into the MRC AML 10 trial. *Blood* 92:2322–2333
3. Sole F, Luno E, Sanzo C et al (2005) Identification of novel cytogenetic markers with prognostic significance in a series of 968 patients with primary myelodysplastic syndromes. *Haematologica* 90:1168–1178
4. Zhang L, Yang W, Hubbard AE et al (2005) Nonrandom aneuploidy of chromosomes 1, 5, 6, 7, 8, 9, 11, 12, and 21 induced by the benzene metabolites hydroquinone and benzenetriol. *Environ Mol Mutagen* 45:388–396
5. Bench AJ, Nacheva EP, Champion KM et al (1998) Molecular genetics and cytogenetics of myeloproliferative disorders. *Baillieres Clin Haematol* 11:819–848
6. Shaffer LG, Tommerup N (2005) Recommendations of the International Standing Committee on Human Cytogenetic Nomenclature. Published in collaboration with 'Cytogenetic and Genome Research'. *International System for Human Cytogenetic Nomenclature*

7. Kor-Anantakul O, suwanrath C, Kannngurn S et al (2006) Prenatal diagnosis of complete trisomy 9: a case report and review of the literature. *Am J Perinatol* 23:131–135
8. Ferreres JC, Planas S, Martínez-Sáez EA et al (2008) Pathological findings in the complete trisomy 9 syndrome: three case reports and review of the literature. *Pediatr Dev Pathol* 11: 23–29
9. Pinette MG, Pan Y, Chard R, Blackstone J et al (1987) Prenatal diagnosis of nonmosaic trisomy 9 and related ultrasound findings at 11.7 weeks. *J Matern Fetal Med* 48–50
10. Póvoa A, Ramalho C, Torgal A et al (2008) Positive biochemical screening for trisomy 18: on the path of trisomy 9. *Prenat Diagn* 28:162–164
11. Mark HF, Gray Y, Sotomayor E (1999) Trisomy 9 in a patient with secondary acute myelogenous leukemia detected by fluorescent in situ hybridization. *Pathobiology* 67:111–114