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Case Report Section

Short Communication

Ring Chromosome 8 as a sole abnormality: An adverse prognostic indicator in Acute Myeloid Leukemia?

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Clinics

Age and sex
70 years old female patient.

Previous history
no preleukemia, no previous malignancy, no inborn condition of note .

Organomegaly
no hepatomegaly, no splenomegaly, no enlarged lymph nodes, no central nervous system involvement

Blood

WBC: 170 x 10^9/l
HB: 11.6g/dl
Platelets: 134 x 10^9/l
Blasts: 95%
Bone marrow: Hyper cellular and replaced by blasts (>90%) having increased nucleo-cytoplasmic ratio with 2 to 3 prominent nucleoli and cytoplasmic granules with strong positivity for myeloperoxidase.

Cyto-Pathology Classification

Phenotype AML M2

Immunophenotype MPO (Strong)

Rearranged Ig Tcr Not performed

Pathology
Increased nucleo-cytoplasmic ratio with 2 to 3 prominent nucleoli and cytoplasmic granules.

Diagnosis AML - M2

Survival

Date of diagnosis 08-2012

Treatment Hydroxyurea.

Complete remission: no

Treatment related death: no

Status Dead

Last follow up 09-2012

Survival 1 month

Karyotype

Sample Bone marrow aspirate**.**

Culture time
Overnight and 24 hours without stimulating agents.

Banding GTG

Results
GTG banding revealed a modal number of 47 with a ring chromosome. Screening of 30 metaphases and analysis of 15 karyotypes confirmed the ring

chromosome as the sole abnormality. Based on the morphology, the ring was suspected to be a ring chromosome 8. Subsequent Spectral Karyotyping confirmed the cytogenetic findings. The final karyotype was reported as: 47,XX,r(8)(p23q24)[30] according to ISCN.

Other molecular cytogenetics technics

Fluorescence in situ hybridization (FISH) using SKYPaint® Probe from Applied Spectral Imaging (Israel), was performed on metaphase chromosomes from cultured Bone marrow sample of this patient and analysed using GenASIs Spectral Karyotyping (HiSKY®) software.

SKY confirmed the marker as a ring chromosome 8.

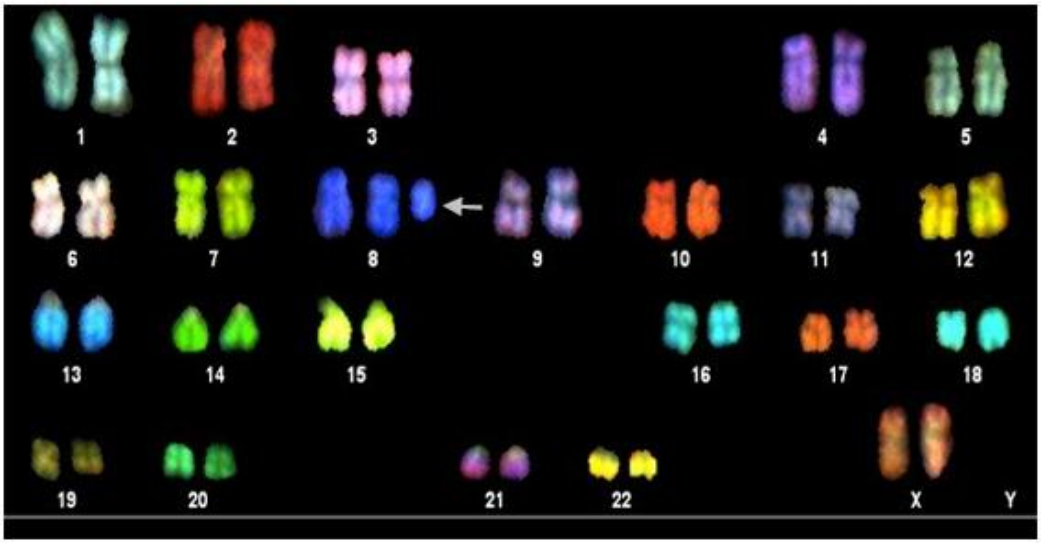

Figure 1: Spectral Karyotyping confirming marker chromosome as Chromosome 8.

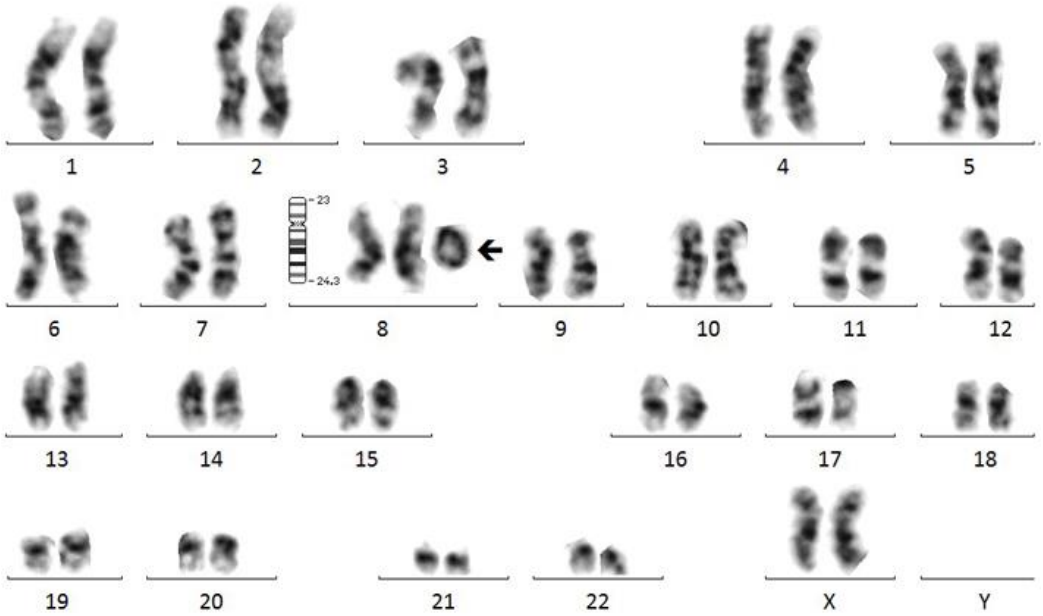

Figure 2: GTG banded karyotype showing Ring chromosome 8.

Comments

A 70-year-old female with AML-M2 was referred for conventional cytogenetic study (CCS) which revealed a modal number of 47 with a ring chromosome. Screening of 30 metaphases and analysis of 15 karyotypes confirmed the ring chromosome as the sole abnormality. Based on the morphology, the ring was suspected to be a r(8). SKY was performed on the sample, which corroborated the cytogenetic findings (Figure 1).

Final karyotype was interpreted as 47,XX,r(8)(p23q24)[30] according to ISCN (Figure 2). Patient was started on Hydroxyurea followed by supportive care and expired within 4 weeks of diagnosis.

Ring chromosomes are a rare entity, which occur in less than 10% of all hematological neoplasm (Gebhart E, 2008). Presence of a ring chromosome

either as part of a complex karyotype or as a sole chromosomal aberration is always in an unbalanced state. This is not only due to the structure of the chromosome, but also the fuctional genes carried in it. The extent to which it is unbalanced can be understood better by molecular tests like FISH and SKY as complementary tests to CCS for better delineation (Gisselsson D et al, 1998). Our case is represented by a partial trisomy of 8 in the form of a ring chromosome. Trisomy 8 is one of the most frequent numerical aberrations in AML, occurring at a frequency 5% as a sole abnormality of all cytogenetically abnormal cases and 10% in cases associated with other aberrations (Heim S, Mitelman F, 2009). As per our knowledge only a few cases of r(8) has been reported either as a sole abnormality (Bibhas Kar et al, 2008) or to be associated with complex chromosomal aberrations in hematological malignancies (F.M. De Oliveria et al, 2007, I Wlodarska et al, 2004, Roland Berger et al, 2002, Gisselsson D et al, 1998, Guiseppina Fugazza et al, 1995)[Table 1].

Table 1: Previous reported cases of ring chromosome 8 in Hematological Malegnancies

Author	Clinical presentation	FAB	Karyotype	Methods	Prognosis
Fugazza G et al, 1996	65 year old male with Parkinson's Disease referred for hemorragic Manifestations.	RAEB-T	46,XY,del(5)(q13q31),t(7 ;20)(q22p13),-8,+r	CCS, Telomeric and centromeric FISH	Patient passed away within 2 months due to sepsis. Unfavourable outcome
Gisselsson D et al, 1998	73 year old Female	AML-M1	45-47,XX,del(5)(q13),-8,+1-2r,+mar[cp15]/72-76,XXX,+5, del(5)(q13)x2,-7,-8,-9,+13,-16,+19,+20,+mar[cp6]/46,XX[4]	CCS, FISH for 8q22	-
Florence Salomon-Nguyen et al, 2000	-	AML-M2	45,X,-X,r(8)	CCS	-
Berger R et al, 2002	19 year female with appendicitis, peritonitis	AML-M2	46,XX,-8,t(8;21),+r	CCS	1yr cytogenetic remission, Favourable outcome
I Wlodarska et al, 2004	71 year old female, Lymphocytosis with massive spleenomegaly CD5-, CD19+, CD22+, CD38 w+, FMC7 +	Small-cell B-NHL	46,XX,t(2 ;11)(p11 ;q13)[7]/46,idem,del(1)(q22q42),r(8)[2]	CCS, FISH for 8p23	Patient passed away due to progressive disease within a year of treatment. Unfavourable outcome
F.M. De Oliveria et al, 2007	41 year old male with lymphadenopathy and hepatosleenomegaly.	T-cell PLL	46,t(X ;14)(q28 ;q11),t(Y ;14)(q12 ;q11),r(8),+mar[20]	CCS,SKY	Patient achived complete regression of lymphadenopathy and hepatosplenomegaly with normal blood count after 5 months of treatment.
Kar B et al, 2008	15 month female with fever, weight loss, gum bleeds and pallor, CD 41 and CD 61 Myeloid blasts present,	AML-M7	46, XX [13]/ 47, XX, +8[2]/ 47, XX, +r (8) [5]	CCS	Patient passed away on day 11 post transplantation, Unfavourable outcome.

Present case study	70 year old female with 95% blasts with Myeloperoxidase positivity.	AML-M2	47,XX,r(8)(p23q24)[30]	CCS, SKY	Patient passed away within 4 weeks of diagnosis, unfavourable outcome.

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