Case Report Section

Short Communication

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

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Published in Atlas Database: August 2016
Online updated version : http://AtlasGeneticsOncology.org/Reports/r8p23q24AshokID100089.html
Printable original version : http://documents.irevues.inist.fr/bitstream/handle/2042/68757/08-2016-r8p23q24AshokID100089.pdf
DOI: 10.4267/2042/68757

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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.

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

Diagnosis AML - M2

Immunophenotype
MPO (Strong)

Rearranged Ig Tcr Not performed

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 functional 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 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 et al, 1998, Guisepina Fugazza et al, 1995). [Table 1].

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

<table>
<thead>
<tr>
<th>Author</th>
<th>Clinical presentation</th>
<th>FAB</th>
<th>Karyotype</th>
<th>Methods</th>
<th>Prognosis</th>
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</thead>
<tbody>
<tr>
<td>Fugazza G et al, 1996</td>
<td>65 year old male with Parkinson's Disease referred for hemorrhagic Manifestations.</td>
<td>RAEB-T</td>
<td>46,XY,del(5)(q13q31),t(7;20)(q22p13),-8,+r</td>
<td>CCS, Telomeric and centromeric FISH</td>
<td>Patient passed away within 2 months due to sepsis. Unfavourable outcome</td>
</tr>
<tr>
<td>Gisselsson D et al, 1998</td>
<td>73 year old Female</td>
<td>AML-M1</td>
<td>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]</td>
<td>CCS, FISH for 8q22</td>
<td>-</td>
</tr>
<tr>
<td>Florence Salomon-Nguyen et al, 2000</td>
<td>-</td>
<td>AML-M2</td>
<td>45,X,X,r(8)</td>
<td>CCS</td>
<td>-</td>
</tr>
<tr>
<td>Berger R et al, 2002</td>
<td>19 year female with appendicitis, peritonitis</td>
<td>AML-M2</td>
<td>46,XX,-t(8;21),+r</td>
<td>CCS</td>
<td>Iyr cytogenetic remission, Favourable outcome</td>
</tr>
<tr>
<td>I Wlodarska et al, 2004</td>
<td>71 year old female, Lymphocytosis with massive spleenomegaly CDS-, CD19+, CD22+, CD38 w+, FMC7 +</td>
<td>Small-cell B-NHL</td>
<td>46,XX,t(2;11)(p11;q13)[7]/46,idem,del(1)(q22q42),r(8)[2]</td>
<td>CCS, FISH for 8p23</td>
<td>Patient passed away due to progressive disease within a year of treatment. Unfavourable outcome</td>
</tr>
</tbody>
</table>
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.

References


Gebhart E. Ring chromosomes in human neoplasias. Cytogenet Genome Res. 2008;121(3-4):149-73


de Oliveira FM, Tone LG, Simões BP, Rego EM, Marinato AF, Jácomo RH, Falcão RP. Translocations t(X;14)(q28;q11) and t(Y;14)(q12;q11) in T-cell prolymphocytic leukemia Int J Lab Hematol 2009 Aug;31(4):453-6

This article should be referenced as such: