Acute basophilic leukemia / t(X;6)(p11;q23)

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Clinics and pathology

Disease
Rare type of acute myeloid leukemia (AML)

Phenotype/cell stem origin
Basophilic precursor.

Epidemiology
Very rare but might be prominent in infants. Four cases of acute basophilic leukemia with t(X;6)(p11;q23) translocation occurring in male infants (< 1 year) have been described.

Clinics
Hyperhistaminemia syndrome has been reported in some of the cases.

Cytology
Major component of undifferentiated blasts and minor component of basophilic blasts containing large granules reacting positively to toluidine blue staining.

Treatment
AML protocols. All patients received standard therapy for childhood AML; Two out of 4 cases reported underwent intrafamilial hematopoietic stem cell transplantation.

Evolution
The 4 patients are still in complete remission, with the following follow-ups: 24 years (P1), 18 years (P2 allografted), 4 years (P3) and 14 years (P4 allografted).

Karyotype of patients at the diagnosis (Patient 1: G-banding; Patient 2 and 3: R-banding). For Patient 3, the chromosome 12 is involved in the rearrangement.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Karyotype at diagnosis / Karyotype revised after FISH analysis (BACs, Fosmids and mBAND)</th>
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</table>
| P1      | 46,Y,t(X;6)(p11;q23)[40]/46,XY[1]
         | der(X)(6qter→6q24::6q23::Xp11→Xq13::6q22q23::Xp11→Xp22::Xq24::Xp22→Xpter),
         | der(6)(6pter→6q22::Xq28→Xq25::Xq23→Xq13::Xpter) |
| P2      | 46,Y,t(X;6)(p11;q23)[29]/46,XY[1]
         | no material available                                                                                                               |
| P3      | 46,Y,der(X)t(X;12)(p21;q23)t(X;6)(q28;q23), der(6)t(X;6)(q28;q23),
         | del(12)(q23)[18]/46,XY[6]
         | der(X)(12qter→12q23::6q22→6q23::Xp11→Xq28::Xp11→Xpter),
         | del(6)(q21q23),del(12)(q23) |
| P4      | 46,Y,t(X;6)(p11;q23)[16]/46,XY[13]
         | der(X)(6qter→6q24::6q23::Xp11→Xq23::Xq25→Xpter),
         | der(6)(6pter→6q23::Xp11→Xp21::Xq24::Xp21→Xpter) |

Table 1. Karyotype at diagnosis.

**Prognosis**
Good response to standard therapy for childhood AML.

**Genetics**

*Note*
One patient had a K-RAS exon 2 mutation (G12S).

**Cytogenetics**

**Cytogenetics morphological**
t(X;6)(p11;q23)

**Cytogenetics molecular**
Molecular cytogenetics (FISH) revealed unbalanced and more complex rearrangements than those observed on karyotype (see Table 1 above).

**Genes involved and proteins**

**MYB**

*Location*
6q23.3

*Protein*
MYB is a transcription factor composed of three domains: an N-terminal DNA binding domain composed of three imperfect repetitions forming a helix-turn-helix structure, a central transactivation domain and a C-terminal negative regulatory domain.

**GATA1**

*Location*  
Xp11.23

*Protein*
GATA1 is a transcription factor composed of an N-terminal activation domain and two zinc-finger domains. GATA1 play an essential role in erythroid differentiation.

**Result of the chromosomal anomaly**

**Hybrid gene**

*Note*
The t(X;6)(p11;q23) resulted in MYB-GATA1 fusion gene.

*Description*
5'MYB-3'GATA1. Breakpoint occurred in the intron 8-9 of MYB and in the intron 4-5 of GATA1.

*Transcript*
The fusion transcript fused the 5’ part of MYB up to exon 8 to the 3’ part of GATA1 from exon 5 to the end.
RP11-104D9 (Red) and RP11-905P20 (Green) span the 5’ part of MYB and the 3’ part of MYB respectively. RP11-104D9 is delocalized onto der(X).

Schematic representation of MYB, GATA1 and MYB-GATA1 proteins. MYB is composed of R1, R2 and R3 which are three imperfect repeats that encompass the DNA-binding domain (DBD) of MYB. TAD is the transactivation domain of MYB and NRD is the negative regulatory domain. GATA1 is composed of an activation domain (AD) and two zinc finger domains. MYB-GATA1 keeps both the DBD and the minimal TAD of MYB and the c-terminal zinc finger domain of GATA1. The breakpoint at the amino acid level is indicated by the blue arrow.
This translocation is associated with loss of expression of wild type GATA1 in leukemic cell due to the involvement of the chromosome X carrying GATA1.

**Fusion protein**

**Description**
The predicted fusion protein comprises the DNA binding domain and the minimal transactivation domain of MYB fused to the DNA binding domain of GATA1.

**Expression / Localisation**
MYB-GATA1 is expressed in the nucleus.

**Oncogenesis**
Expression of MYB-GATA1 in mouse hematopoietic progenitors committed them to the granulocyte lineage, blocked them at an early stage of differentiation and transformed these cells.

**References**


This article should be referenced as such: