Leukaemia Section
Short Communication

t(8;16)(p11;p13) KAT6A/CREBBP
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Abstract
Review on t(8;16)(p11;p13) KAT6A/CREBBP, with data on clinics, and the genes implicated.

Clinics and pathology

Disease
Acute myeloid leukemia (AML) including AML-M4, AML-M5a/M5b; Treatment related AML (t-AML).

Note
In t-AML with t(8;16), patients often had a previous history of solid tumour (breast cancer) or haematological diseases (CML, lymphomas).

Phenotype/cell stem origin
AML with t(8;16) may arise from an early stem cell with myeloid and monoblastic differentiation potential.

Epidemiology
Rare disease: a hundred and twenty cases have been reported in Mitelman database; (<1% of AML); found in children (median age at diagnosis: 1.2 years) and adults (median age at diagnosis: 59.4 years) with a female predominance (2/3).

Clinics
Disseminated intra vascular coagulation may be present; extramedullary infiltration; 20% of the cases could be therapy-related.

Cytology
Blast cells present a myelomonocytic stage of differentiation, and are characterized by a phenomenon of erythroagglutination with strong peroxidase and esterase activities. Immunophenotyping reveals CD4, CD14, CD13, CD33, CD56 and HLA-DR positives; CD34, CD117 and CD133 negatives.

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The t(8;16) has been cloned and shown to fuse the MOZ (monocytic leukemia zinc finger) gene at 8p11.2 to the CBP (CREB binding protein) gene at 16p13.3. The MOZ gene has also been found to be involved in variant translocations t(8;19)(p11;q13) and t(8;22)(p11;q13) and inv(8)(p11q13) translocations associated with M5/M4 AML. This translocation is associated with AML M5/M4. In the majority of cases it is associated with features of hemophagocytosis by leukemic cells, particularly erythrophagocytosis - Text and iconography Courtesy Georges Flandrin 2001.
Prognosis

The prognosis is poor. In published series, death of patients occurs in half of the cases during the first 10 months after diagnosis due to infections or bleeding; survival is often less than 1 year but spontaneous remission has occurred (at least) once.

Cytogenetics

Additional anomalies

Sole anomaly in 53.3% of cases; in 23.3% of cases, single additional abnormality: +8, various; in 23.3% of cases: complex karyotype; rare chromosome 7 abnormalities, often in t-AML.

Variants

Complex variant t(8;16;V) may occur and has been described on rare occasions. 8p11 may have other partners: t(8;22)(p11;q13) which involve EP300 in 22q13, EP300 is a homologue of CREBBP with acetyltransferase activity; t(8;19)(p11;q13.3) which should involve LEUTX on 19q13 (found in one t-AML case); inv(8)(p11p13) which leads to MYST3- NCOA2 fusion; t(8;20)(p11;q13) leading to MYST3- NCOA3 fusion.

Genes involved and proteins

**KAT6A**

Location
8p11

Note
KAT6A is also known as MYST3, or MOZ (monocytic leukemia zinc finger).

DNA/RNA
KAT6A gene is composed of 17 exons, with a MYST domain, located in exons 9-14, that remains intact in the (8;16) translocations.

Protein
KAT6A gene encodes for a nuclear protein with histone acetyltransferase (HAT) due to MYST domain, and transcriptional regulator activities.

**CREBBP**

Location
16p13

Note
CREBBP is also known as CBP.

DNA/RNA
CREBBP is composed of 31 exons.

Protein
The protein encoded shows intrinsic histone acetyltransferase activity and shares regions of very high sequence similarity with protein p300.

Result of the chromosomal anomaly

**Hybrid gene**

Description
5' KAT6A - 3' CREBBP or 5' CREBBP - 3' KAT6A.
**Transcript**

Five KAT6A-CREBBP transcripts have been described: type I (KAT6A exon 16-CREBBP exon 3); type II (KAT6A exon 16-CREBBP exon 4); type III (KAT6A exon 17-CREBBP exon 2 or 4); type IV (KAT6A exon 15-CREBBP exon 4); type V (KAT6A exon 15-CREBBP exon 5). Type I transcript is the most frequent fusion product. Reciprocal transcripts CREBBP-KAT6A: type I (CREBBP exon 2-KAT6A exon 17); type IV (CREBBP exon 3-KAT6A exon 16) are also found.

**Fusion protein**

Description

The breakpoint for KAT6A is amino acid 1.013 or amino acid 1.117 (in the acidic domain). Fusion protein loses part of acidic domain in C-terminal. HAT domains in KAT6A and CREBBP are conserved.

Oncogenesis

t(8;16) AML are characterized by overexpression of HOXA9, HOXA10, and MEIS1; upregulation of RET and PRL; downregulation of CCND2, STAT5 and WT1. They share similarities with MLL-rearranged leukemias suggesting a partially common leukemogenic pathway.

**References**


This article should be referenced as such: