Leukaemia Section
Short Communication

\[ t(5;17)(q35;q21) \]

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Clinics and pathology

**Disease**
Acute non lymphocytic leukemia (ANLL).

**Phenotype/cell stem origin**
Acute promyelocytic leukemia (ANLL-M3 according to the FAB classification).

**Etiology**
Exceptional; only 2 well documented cases.

**Clinics**
Both patients were pediatric cases: F/2.5 years, M/12 years; disseminated intravascular coagulation at diagnosis in one case; remission obtained with chemotherapy and/or ATRA; first relapse at 7 and 5 months respectively.

**Cytology**
Hypergranular and hypogranular bilobed promyelocytes; absence of Auer rods; typical microspeckeled pattern with anti-RARa antibodies; terminal differentiation of blasts and promyelocytes in vitro with ATRA.

**Prognosis**
Probably unfavorable (both patients had a short term first relapse).

**Cytogenetics**

**Probes**
RARa probe commercially available coupled with PML probe in dual color kits; non commercialized probes for NPM, previously used for \( t(2;5)(p23;q35) \) of anaplastic large cell lymphoma (same breakpoint into NPM) = cosmid clones 13, 15-2 and 47C12 retained by der(5).

**Additional anomalies**
One of the two cases had complex additional abnormalities.

**Variants**
\( t(15;17)(q22;q21) \) \( t(11;17)(q23;q21) \) \( t(11;17)(q13;q21) \)

**Genes involved and proteins**

**NPM1**

- **Location**
  5q35

- **Protein**
  Gene for the nucleolar phosphoprotein nucleophosmin; would participate in ribosome assembly.

**RARa**

- **Location**
  17q21

- **Protein**
  Gene for the retinoic acid receptor alpha; the breakpoint lies within the second intron of the gene, as in \( t(15;17) \) and \( t(11;17) \) translocations.

**Result of the chromosomal anomaly**

**Hybrid gene**

**Description**
Two reciprocal fusion genes are generated: 5'-NPM + 3'-RARa on der(5) and 5'-RARa + 3'-NPM on der(17); both fusion genes are transcribed, the crucial one is NPM-RARa; two NPM-RARa chimeric cDNAs are generated, one short and one long differing from 129 bp, with corresponding transcripts of 2.3 and 2.4 kb (alternatively spliced transcripts); in one case, only the
short NPM-RARα isoform could be detected; the 5' end of NPM-RARα cDNAs contains the first 442 bp of the NPM cDNA; the 3' end contains RARα sequences of exon 3 through the 3' end of RARα; a reciprocal RARα-NPM transcript is detected: RARα exons 1 and 2 are fused to 3' NPM downstream bp 443.

**Detection**
Nested RT-PCR.

**Fusion protein**
Description
Two NPM-RARα proteins, of 563 and 520 amino acids, are encoded (MW 62 and 57 kDa); NPM-RARα fusion protein acts as a retinoic acid-responsive transcriptional activator: increase of activity in a concentration dependant manner.

**References**


Redner RL, Corey SJ, Rush EA. Differentiation of t(5;17) variant acute promyelocytic leukemic blasts by all-trans retinoic acid. Leukemia. 1997 Jul;11(7):1014-6


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