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Leukaemia Section

Mini Review

t(1;21)(p36;q22)

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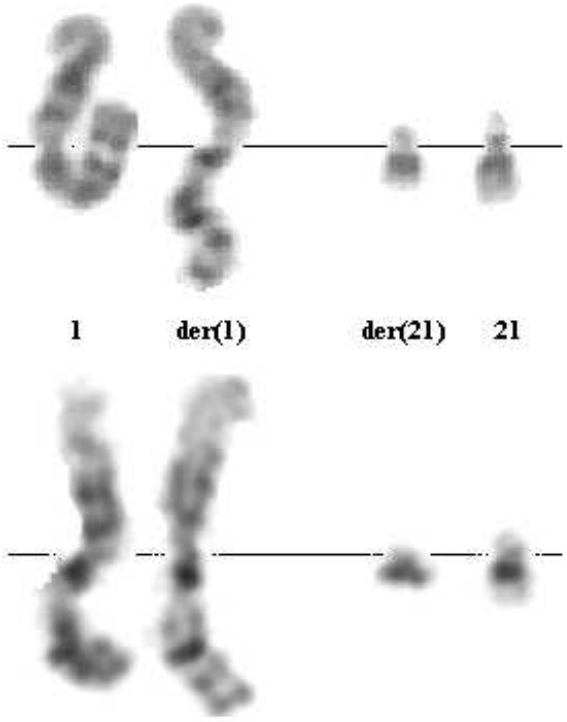
Identity

Note: Subtle cytogenetic abnormality, easy to confuse with a del(21)(q22), may be missed in poor quality metaphases.



Partial GTG-banded karyotype of t(1;21)(p36;q22).

Age/Sex	Diagnose	Survival (mths)	Karyotype	Previous therapy
60/M	AML-M1	7	46,XY,t(1;21)(p36;q22)[12]	chemotherapy (a)
8/F	RAEBt	6	46,XX,t(1;21)(p36;q22),-7,+mar	none reported
72/M	MDS/AML-M2	6	46,XY,t(1;21)(p36;q22)	exposure to nuclear explosions
72/F	AML-M4	>2	46,XX,t(1;21)(p36;q22)[20]	none reported
47/F	AML-M0	7	46,XX,t(1;21)(p36;q22)[10]	radiotherapy + chemotherapy (b)

(a) lomustine, vincristine, cyclophosphamide, etoposide;
(b) fluorouracil, epirubicin, cyclophosphamide.

Clinics and pathology

Disease

Acute non lymphocytic leukemia (ANLL or AML: acute myeloid leukemia) and myelodysplastic syndromes (MDS); 2 of 5 cases at least are secondary to toxic exposure**.**

Note: Only 5 cases described so far one with features identical to a case of TXT t(18;21)(q21;q22), and a case of t(19;21)(q13.4;q22).

Etiology

Two of the reported cases are therapy-related, in another case, ANLL occurred about 50 years after radiation exposure from nuclear explosions.

Prognosis

Poor; median survival 6 months.

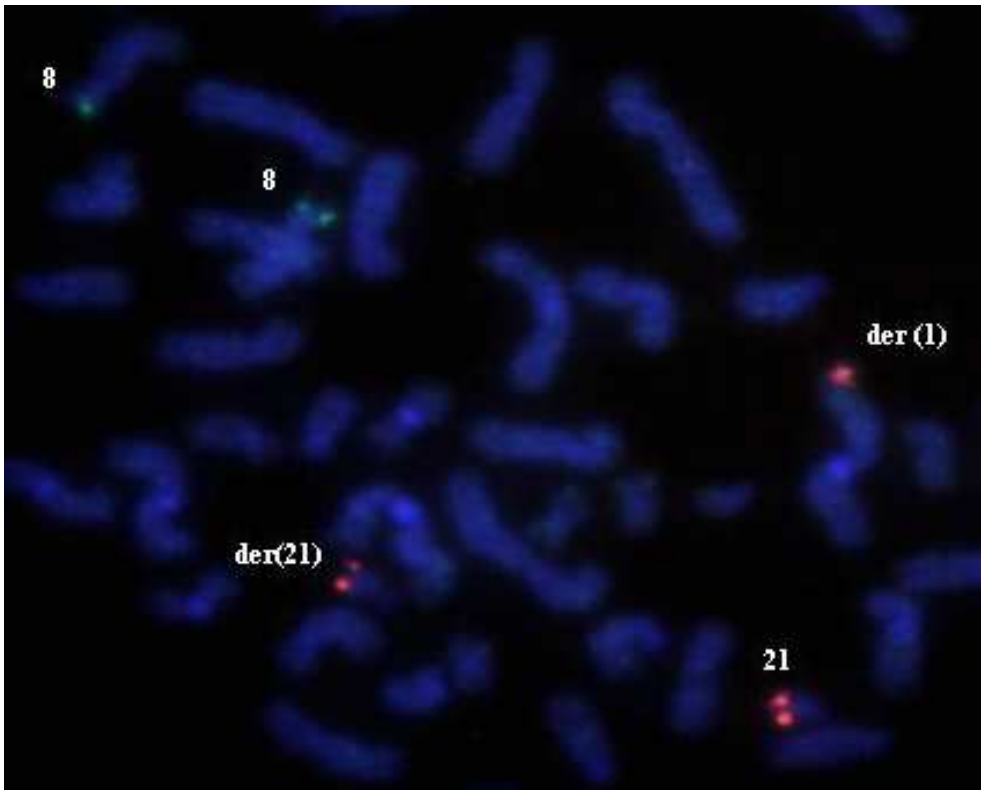
Cytogenetics

Probes

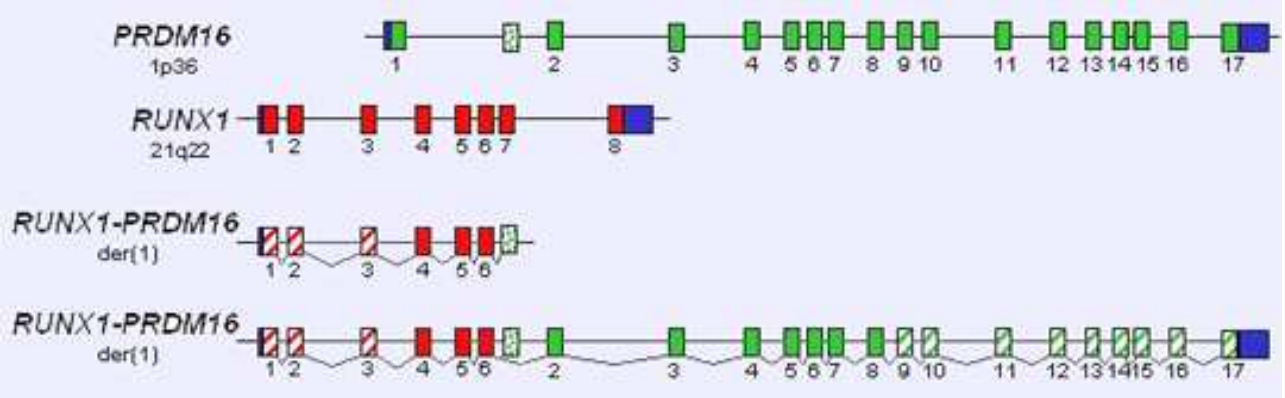
AML1/ETO dual-color, dual-fusion probe.

Additional anomalies

-7, del(7q).



FISH analysis using RUNX1 (red) probe. Three signals for RUNX1 are observed; on the normal chromosome 21, and on the derivative chromosomes 1 and 21.



Schematic representation of RUNX1 and PRDM16 (fusion) genes.
Upper panel: normal genomic structures of PRDM16 and RUNX1 (non-coding parts in bleu). A cryptic exon, residing within intron 1 of PRDM16, is indicated in green (speckled).
Lower panel: structure of RUNX1-PRDM16 fusion transcripts. Exons are numbered on the basis of consensus gene sequences. Exon sizes are not to scale.

Genes involved and Proteins

PRDM16

Location: 1p36
Note: This gene is also involved in the t(1;3)(p36;q21) (AML/MDS).

Protein

Zinc-finger protein, containing two DNA binding domains and a PRDI-BF1 (positive regulatory domain I binding factor 1/ RIZ (retinoblastoma-interacting zinc finger protein) homologous (PR) domain at the N-terminus.

RUNX1/AML1

Location: 21q22

DNA / RNA

Transcription is from telomere to centromere.

Protein

Contains a Runt domain and, in the C-term, a transactivation domain; forms heterodimers; widely expressed; nuclear localisation; transcription factor (activator) for various hematopoietic-specific genes.

Results of the chromosomal anomaly

Hybrid gene

Note: Two different chimeric transcripts have been identified. One contains the exon 1 to 6 of RUNX1 including the runt domain, fused to sequences derived from intron 1 of PRDM16. The other fusion transcript contains exons 1 to 6 of RUNX1 and almost the entire PRDM16 coding region (see figure above).

Description

5' RUNX1 - 3' PRDM16.

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