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Leukaemia Section
Short Communication

inv(11)(q13q23)

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Clinics and pathology

Disease

Infant acute lymphoblastic leukemia (ALL)

Epidemiology

Poorly defined, only one case described to date, a 9-months-old boy with Pro-B ALL (FAB L1) (Alonso et al., 2010).

Evolution

Patient achieved complete remission on day 33 of treatment and 5 months since diagnosis presented a bone marrow relapse.
The patient had no available compatible donor and he did not receive a second line treatment and palliative care was administered.
He died due to progressive disease.

Prognosis

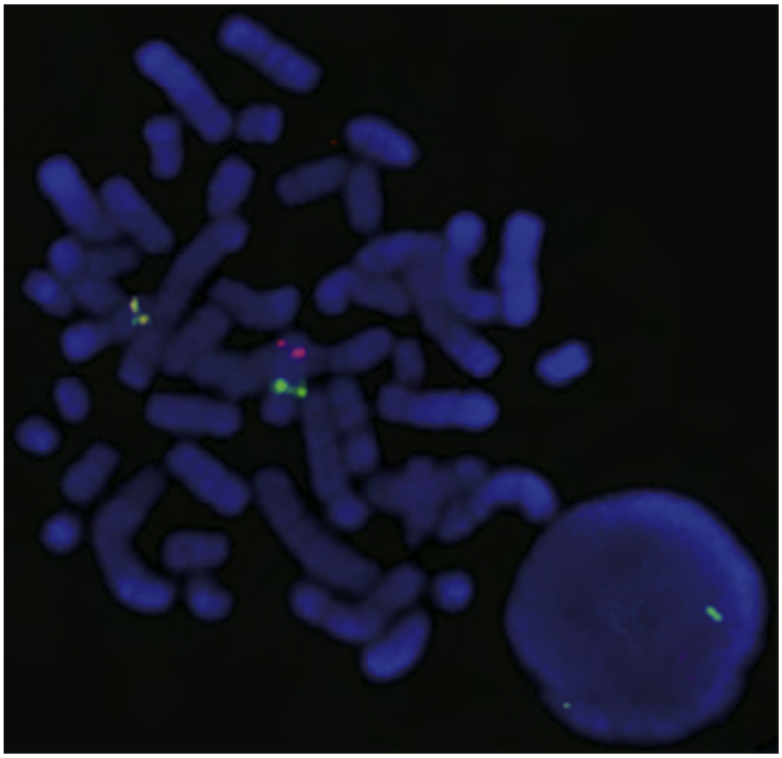
Infant-ALL with 11q23 abnormality/MLL gene rearrangement has been defined as a type of leukemia with poor prognosis (Pieters et al., 2007). The patient relapsed at +5 months and died due to progressive disease.

Genetics

Note

Fusion gene MLL-BTBD18 (Alonso et al., 2010) was detected by LDI-PCR, as described (Meyer et al., 2005).

Partial G-banded karyogram for the inv(11)(q13q23), showing both chromosomes 11.



Split-FISH: The hybridization pattern for the chromosome with the MLL-BTBD18 rearrangement is one red/one green signal, while the yellow signal represents the germline MLL allele.

Cytogenetics

Cytogenetics morphological

46,XY,inv(11)(q13q23) as sole abnormality.

Cytogenetics molecular

Split-FISH analysis revealed two signals corresponding to the 3' and the 5' probes, both on the long arm of chromosome 11 (Alonso et al., 2010).

Probes

MLL Dual Color Break Apart Rearrangement Probe.

Genes involved and proteins

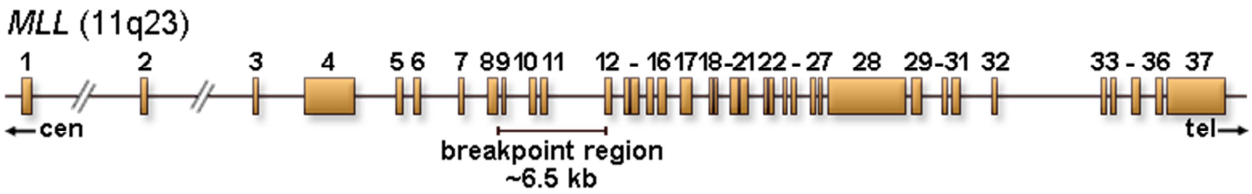
MLL

Location

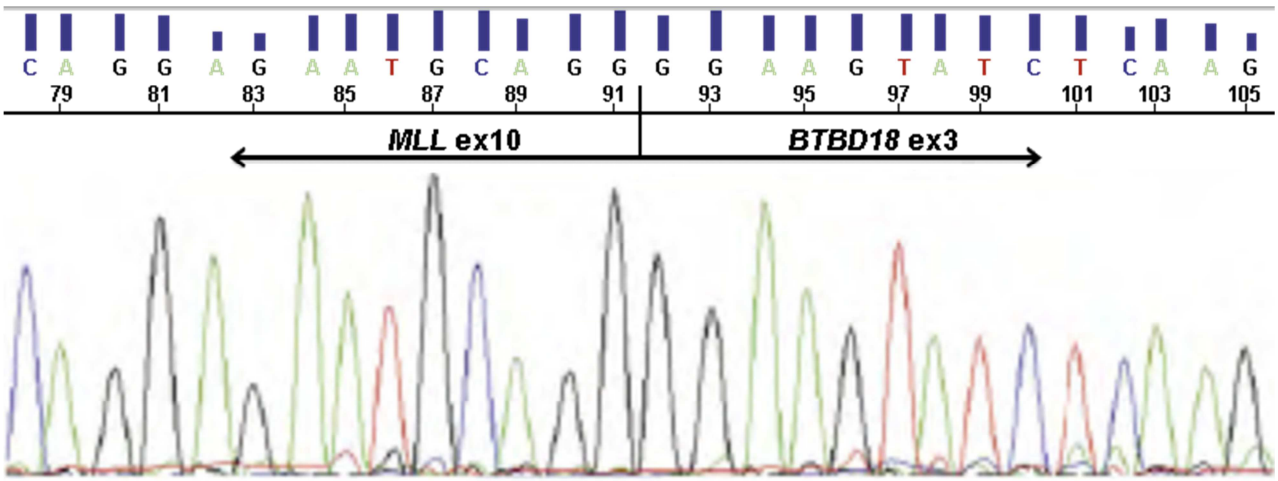
11q23

DNA/RNA

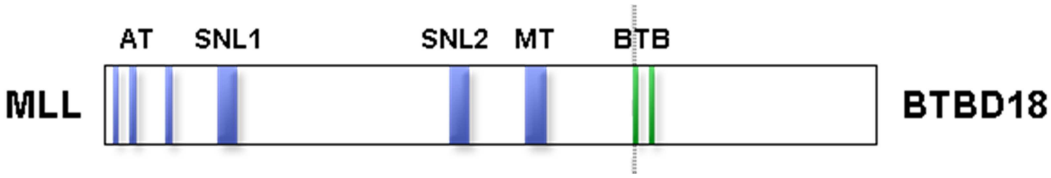
The Mixed-Lineage Leukemia gene consists of at least 37 exons, encoding a 3969 amino-acid nuclear protein with a molecular weight of nearly 431 kDa.



Schematic diagram of the exon/intron structure of the MLL gene (Nilson et al., 1996).



Fusion sequence of the MLL-BTBD18 fusion transcript.



Schematic diagram of the structure of the predicted MLL-BTBD18 fusion protein.

Protein
431 kDa; contains two DNA binding motifs (a AT hook and Zinc fingers), and a DNA methyl transferase motif; wide expression; nuclear localisation; transcriptional regulatory factor.

BTBD18

Location
11q12.1

Protein
712 amino acids; 78 kDa.

Result of the chromosomal anomaly

Hybrid gene

Description
In frame fusion between the truncated MLL exon 10 and the truncated BTBD18 exon 3.

Transcript
MLL-BTBD18.

Detection
RT-PCR (van Dongen et al., 1999; Alonso et al., 2010).

Fusion protein

Description
Fusion protein of 1989 amino acids containing 1374 codons from the amino-terminal region of MLL and 614 codons from the carboxy terminal portion of the BTBD18 protein, plus "fusion codon" consisting of two nucleotides derived from the MLL gene sequence and one from BTBD18 gene sequence. The chimeric protein of 1989 amino acids retains a major portion of MLL, including those domains known to be essential for leukemic transformation: the AT-hooks and the DNA methyltransferase domain (DNMT). The C-terminal sequences are derived from the BTBD18 protein, a new fusion partner. The fusion occurred with in the BTB/POZdomain of BTBD18 (Alonso et al., 2010).

To be noted

Note
Additional cases are needed to delineate the epidemiology and prognosis of this entity, even when MLL abnormalities are associated with poor prognosis, especially when they are identified in infant leukemias (Pieters et al., 2007).

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