

# Leukaemia Section

## Mini Review

### t(14;19)(q32;q13) IGH/CEBPA

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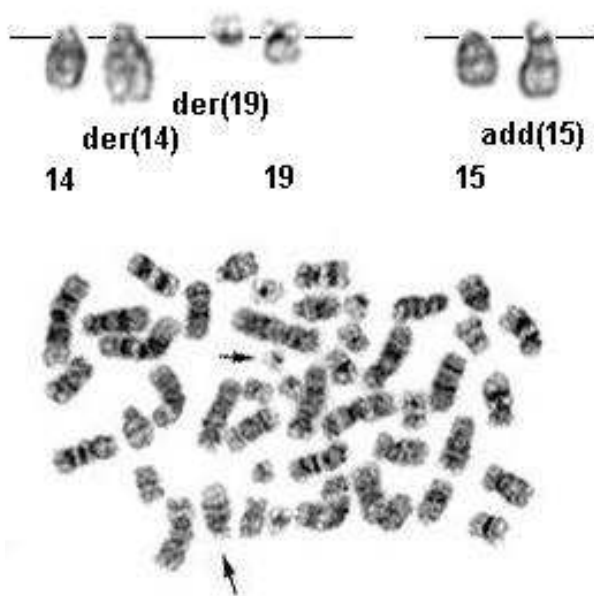
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#### Identity

##### Note

This abnormality is cytogenetically identical but molecularly distinct from the t(14;19)(q32;q13) seen in chronic lymphoid leukaemia (CLL) and other chronic B-cell lymphoproliferative disorders, which results in the juxtaposition of BCL3 with IGH on the der(14) and subsequent over expression of the BCL3 protein.



G-banded metaphase showing the t(14;19)(q32;q13). The derivative chromosomes 14 and 19 are arrowed (bottom) G-banded karyogram showing the t(14;19)(q32;q13) and a add(15q) (top).

#### Clinics and pathology

##### Disease

Acute lymphoblastic leukaemia (ALL).

##### Phenotype/cell stem origin

B-lineage immunophenotype and FAB L1, mostly CD10+: B-cell precursor acute lymphoblastic leukemia (BCP-ALL).

##### Epidemiology

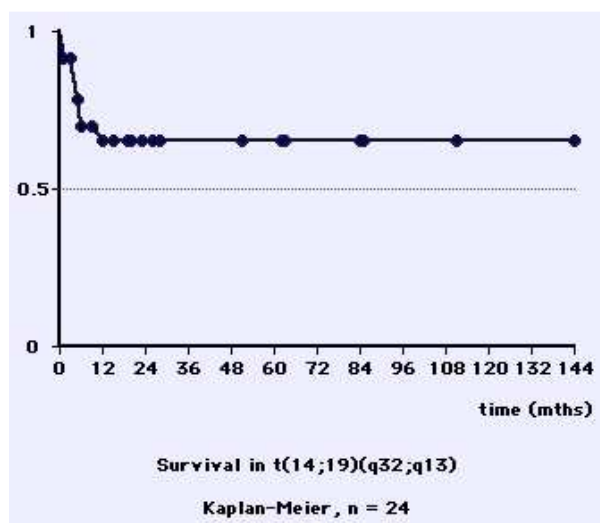
Rare, with only 28 cases reported to date (Heerema et al., 1985; Prigogina et al., 1988; Pui et al., 1993; Andreasson et al., 2000; Robinson et al., 2004; Chapiro et al., 2006; Akasaka et al., 2007). The estimated incidence in childhood and adult ALL is <1%. Among the reported cases there appears to be a female predominance (9M/19F) which is unusual for ALL. The age range of patients is 5 to 76 years with a median of 19 years. This abnormality is most often found in adolescents and young adults.

##### Clinics

Typically, patients with this abnormality have low white cell count of 9/L, but 10% of patients present with a WBC above 50 x 10<sup>9</sup>/L.

##### Prognosis

It is difficult to assess the true prognosis of patients with this abnormality given its rarity, however initial data suggest that the prognosis is better than expected for patients of a similar age (see Figure 2).



## Cytogenetics

### Note

This balanced translocation can usually be identified by G-banding alone. The breakpoint on chromosome 14 is consistently given as 14q32; however the breakpoint on chromosome 19 has, in the past, been more variably attributed, from q11 to q13. It is to be noted, however, that the gene involved on chromosome 19, CEBPA, lies at 38,482,776 bp from pter, very close to the q12 band limit.

### Cytogenetics morphological

The t(14;19) has been described as the sole abnormality in 12 out of 28 cases, and is more frequently accompanied by additional structural and/or numerical abnormalities; +21 (acquired) was found in three cases, +6 in two cases. A t(9;22)(q34;q11) was found in one case, a trisomy 8 in one case.

This abnormality has been reported in a single case with Down syndrome. In a closely related translocation, the t(8;14)(q11;q32) with CEBPD/IGH involvement, more than 1/4 of cases were Down syndrome patients.

## Genes involved and proteins

### Note

The involvement of the IGH gene located at 14q32 has been demonstrated via FISH using the LSI IGH Dual Colour Break Apart Rearrangement Probe in all cases tested. Metaphase and interphase FISH using probes flanking the BCL3 gene have ruled out the involvement of this gene; thus distinguishing it from the cytogenetically identical translocation t(14;19)(q32;q13) seen in CLL and other chronic B-cell lymphoproliferative disorders.

### IGH

#### Location

14q32

## CEBPA

### Location

19q13

### Note

Alternatively, CEBPG can be involved instead of CEBPA (one case so far described). It is unknown if they bear the same prognosis, as they differ in their N-term.

### DNA/RNA

CEBPA is a single-exon gene, CEBPG also.

### Protein

DNA-binding protein. CCAAT enhancer-binding protein (CEBP) transcription factors are a family of 6 multifunctional basic leucine zipper (bZIP) transcription factors. The 4 other CEBPs are: CEBPB (20q13), CEBPD (8q11), CEBPE (8q11), all three equally implicated in leukemias, and DDIT3/CHOP/CEBP zeta (12q13), so far known to be involved in solid tumours (liposarcoma). These transcription factors play a key role in cellular differentiation, in particular in the control of myeloid differentiation. CEBPA is composed of an N-term transactivation domain, a negative regulatory domain, a DNA-binding basic motif, and a leucine-zipper domain in C-term. CEBPA mRNA is translated into two major proteins, p42CEBPA and p30CEBPA. The 30 kDa protein lacks the transactivating domain, and inhibits DNA binding and transactivation by p42CEBPA. CEBPA is essential for the lineage specific differentiation of myelocytic haematopoietic precursors into mature neutrophils. CEBPG only contains a DNA-binding basic motif, and a leucine-zipper domain (Ramji et al., 2002; Nerlov et al., 2007).

### Germinal mutations

CEBPA has been found mutated in a familial acute myeloid leukemia (Smith et al., 2004).

### Somatic mutations

10% of acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS) cases exhibit a mutation in CEBPA. It seems to bear a good prognosis

## Result of the chromosomal anomaly

### Fusion protein

#### Oncogenesis

Overexpression of the CEBP gene.

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