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Leukaemia Section

Mini Review

t(14;19)(q32;q13)

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Identity

Note

The t(14;19)(q32.3;q13.2) is a rare but recurrent translocation found in patients with B-cell malignancies, mainly in chronic B-cell lymphoproliferative disorders. When occurring in chronic lymphocytic leukaemia (CLL), atypical lymphocyte morphology and immunophenotype have been reported.

Clinics and pathology

Disease

Chronic lymphocytic leukemia (most are the atypical form). Other diseases (maybe less well defined): low grade B-NHL, mantle cell lymphoma, small non-cleaved cell lymphoma, one case of biphenotypic (B/M) acute leukemia.

Phenotype/cell stem origin

Chronic B-cell lymphoproliferation.

Epidemiology

Annual incidence $30/10^6$; median age: 60-80 years; A high proportion of patients with CLL and t(14;19) are aged less than 40 years.

Clinics

Often a slow evolutive disease.

Prognosis

Highly variable according to the staging: from staging A: where the survival is not reduced compared to age matched population, to staging C: with a median survival of 2 years. t(14;19) is often associated with rapidly progressive disease, and overall prognosis is poor compared to the expected survival in chronic lymphocytic leukemia and low-grade B-cell lymphoma.

Cytogenetics

Cytogenetics morphological

The t(14;19)(q32.3;q13.2) is reciprocal and results in 14q+ and a 19q- derivative chromosomes.

Cytogenetics molecular

FISH is useful for identifying variant translocations.

Additional anomalies

t(14;19) is rarely the sole cytogenetic aberration. Trisomy 12 is the most frequent associated abnormality, and is observed in 50% of cases; this may even be underestimated as with FISH more cases with +12 are detected. Other chromosomes involved in structural aberrations are 6, 2 and 10.

Variants

Three way variants are relatively frequent, compared to variants in other recurrent translocations. t(14;17;19) and t(7;19;14) were described.

Genes involved and proteins

IgH

Location

14q32

BCL3

Location

19q13

DNA/RNA

9 exons, spanning 11.5 kb. BCL3 mRNA is expressed in a variety of tissues, particularly in spleen, liver and lung.

Protein

- Encodes the a protein which contains seven ankyrin repeats. Similar repeats are described in the structural

protein ankyrin, as well as in proteins involved in cell cycle control and lineage determination (SW14, SW16, lin2).
- BCL3 is a member of the IkappaB family, whose proteins regulate the NFkappaB family of transcription factors. NFkappaB plays a major role in B-cell development.

Result of the chromosomal anomaly

Hybrid gene

Description

The breakpoint is located in the 5' untranslated region of the BCL3 gene. BCL3 is juxtaposed to the immunoglobulin heavy chain gene locus on chromosome 14 (often in the switch alpha region) in a "head-to-head" configuration.

Fusion protein

Oncogenesis

- No fusion protein. The translocation does not interrupt the transcriptional integrity of BCL3, but is associated with increased production of a BCL3 RNA of normal size. The immunoglobulin enhancer is not present on the same derivative chromosome as BCL3, suggesting other mechanisms for overexpression.
The genes affected by overexpression of BCL3 remain to be identified.

References

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