Leukaemia Section
Mini Review

+12 or trisomy 12
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Identity

Note: Trisomy 12 is the most common cytogenetic change in chronic lymphocytic leukemia (CLL); however, it has also been observed in other subtypes of B-cell lymphoproliferative disorders, where it is not seldomly a secondary change.

Clinics and pathology

Disease
B-cell chronic lymphocytic leukemia (B-CLL).

Phenotype/cell stem origin

virgin CD5+ recirculating B-cell; the classical CLL phenotype is CD5+, CD23+, CD22-, CD79a-, FMC7-, slg weak; trisomy 12 is more often observed in CLL with morphologically and immunologically atypical cells, displaying CD5 negativity or FMC7 positivity and strong surface immunoglobulin staining; trisomy 12 is present in proliferating cells and seems to be associated with the absence of mutation of the Ig variable region genes.

Epidemiology

Trisomy 12 is found in one third of cytogenetically abnormal CLLs by conventional karyotype, and in about 12-54% of cases when interphase FISH is used.

Prognosis

A significant difference comparing the therapy-free interval of patients with +12 and patients with other anomalies was found; this observation was repeatedly confirmed; however an adverse impact of +12 on survival could not be demonstrated until the IWCLL compiled karyotype and survival data from more than 400 patients and showed a median survival of 5.4 years versus 8.6 years versus 14 years in patients with +12 versus another single abnormality versus a normal karyotype, respectively; the preliminary results on a large series of patients analyzed by interphase FISH showed that +12 and 14q+ changes are associated with shorter survival times, compared to patients with 13q abnormalities and normal karyotypes; however prospective data are needed to further assess the prognostic value of this cytogenetic change.

Disease
B-cell non Hogkin's lymphomas, distinct from CLL, i.e. polymphocytic leukemia, hairy cell leukemia, splenic lymphoma with villous lymphocytes (SLVL), Waldenström's disease, follicular lymphoma, mantle cell lymphoma, and diffuse large cell lymphoma.

Phenotype/cell stem origin

Lack of specificity for a particular immunophenotype.

Prognosis

No data are available concerning the prognostic significance of +12, except in one series of mantle cell lymphomas in which it was the only single cytogenetic parameter associated with poor prognosis.

Cytogenetics

Cytogenetics morphological

Using restriction fragment length polymorphism analysis, the extra chromosome 12 has been shown to derive from duplication of one chromosome 12, with retention of the other homolog rather than from triplication of one homolog; trisomy 12 is thought to be a secondary change since combined immunological and cytogenetic studies showed that it is present in only a part of the neoplastic B-cells; cases with partial duplication 12q were analyzed by FISH, and a "minimal duplicated region" could be defined in segment 12q13-12q15.
References


Hamblin TJ, Davis Z, Gardiner A, Oscier DG, Stevenson FK. Unmutated Ig V(H) genes are associated with a more aggressive form of chronic lymphocytic leukemia. Blood. 1999 Sep 15;94(6):1848-54

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