Classification of B-cell chronic lymphoproliferative disorders (CLD)

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Identity

Note: A classification of chronic (mature) B-cell lymphoproliferative disorders based on reproducible morphologic and immunologic criteria was proposed by the FAB group in 1989. Ever since a number of cytogenetic studies disclosed a remarkable degree of heterogeneity within each disease category. Herein, the main cytogenetic entities of chronic lymphocytic leukemia and related disorders, B-cell prolymphocytic leukemia, splenic lymphoma with villous lymphocytes are presented.

Other disease subsets of B-cell CLD include the leukemic phase of follicle centre cell lymphoma, mantle cell lymphoma and lymphoplasmacytic lymphoma. The cytogenetic features of these forms of leukemic lymphoma are described in the B-NHL classification.

Comment: The incidence for each of these chromosome lesions (below) is higher when investigated by the more sensitive fluorescence in situ hybridization (FISH) technique. FISH detected 13q deletion in 40-50% of the cases, +12 in 15-20% of the cases; 11q deletion in 7-10% of the cases; 17p deletion in 15-20% of the cases. The prognostic significance for each of these anomalies, 11q-excluded, mainly derives from studies that used conventional cytogenetics and needs to be reassessed in the light of the more recent data provided by FISH analysis.

Legend for immunophenotypes (below): +: positive in >90% of the cases; +/-: positive in more than 50% of the cases; -/+: positive in less than 50% of cases; -: negative in <10% of the cases; pan-B markers include CD19; CD20; CD79a R = rearranged; sIg: surface immunoglobulins; cyIg: cytoplasmic Ig; IgV genes: genes encoding for the variable portion of the Ig. MTC and mTC1: major translocation cluster and minor translocation cluster 1 of BCL1 region, respectively.

Clinics and pathology

Disease

Chronic lymphocytic leukemia CD5+ B cell that has encountered the antigen and harbours hypermutated IgV genes.

Phenotype/cell stem origin

CD5+; CD23+; CD38+/−; CD22 weak+; FMC7−; sIg+ weak.

Cytogenetics

del(13q) (10-15% of the cases): Typical morphology; indolent disease; favourable prognosis if present as the sole change (Note: typical morphology (FAB criteria): more than 90% of neoplastic cells are represented by small lymphocytes (diameter less than 14 m, i.e. < two red blood cells); atypical morphology: 10-55% of the lymphocytes are larger than 14 m with few prolymphocytes (CLL mixed-cell type); the cases are usually referred to as CLL/PL if prolymphocytes predominate among large lymphoid cells; PLL: more than 55%, and usually >70% of the cells are prolymphocytes.).

Disease

Chronic lymphocytic leukemia CD5+ virgin recirculating B-cell with germline IgV genes.

Phenotype/cell stem origin

CD5+; CD23+; CD38-/++; CD22 weak+; FMC7−; sIg+ weak.
**Cytogenetics**

+12 (10-15% of the cases): Frequent atypical morphology; relatively indolent disease; unfavourable prognosis as compared with other single chromosome aberrations, but not against complex karyotypes, 11q- or 17p-.

**Disease**

Chronic lymphocytic leukemia CD5+ recirculating B-cell.

**Phenotype/cell stem origin**

CD5+; CD23++; CD22 weak+; FMC7--; sIg+ weak.

**Cytogenetics**

11q22-23 deletion (ATM gene involved) (5-6% of the cases): Usually typical morphology with karyotype instability; Relatively aggressive disease, with development of multiple adenopathies; Unfavourable prognosis.

del(17p) (p53 gene involved) (<5% of the cases): Morphology consistent with CLL/PL Advanced disease; Refractoriness to purine analogs; Unfavourable prognosis.

t(11;14)(q13;q32) (BCL1 involved in the MTC and mTC1) (<5% of the cases): Rare cases of CLL/PL, transforming into prolymphocytic leukemia; Primary blood and marrow involvement, usually with splenomegaly, without adenopathy.

**Disease**

Prolymphocytic leukemia (PLL).

**Phenotype/cell stem origin**

Peripheral B-lymphocyte that has encountered the antigen and harbours hypermutated IgV genes.

**Clinics**

Rare and aggressive disease with a majority of relatively large lymphocytes with round nucleus and a prominent central nucleolus.

**Cytogenetics**

t(11;14)(q13;q32) (BCL1 involved in the MTC and mTC1).

**Disease**

Splenic lymphoma with villous lymphocytes.

**Phenotype/cell stem origin**

Marginal zone lymphocytes harbouring hypermutated IgV genes.

Pan-B+; CD5-/++; CD23-/++; CD11c+/--; CD25-/++; FMC7+/--; sIg+ bright.

**Clinics**

Indolent disease; There are not established correlations between chromosome lesions and hematologic features; Cases with t(11;14) showed frequent CD5-positivity and featured an indolent course.

**Cytogenetics**

(20% of the cases) (breaks outside the MTC and mTC1 of BCL1).

(20-40% of cases) with or without +3.

**References**


Naylor M, Capra JD. Mutational status of Ig V(H) genes provides clinically valuable information in B-cell chronic lymphocytic leukaemia. Blood. 1999 Sep 15;94(6):1837-9


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