

Classification of B-cell chronic lymphoproliferative disorders (CLD)

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 the 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 13q14 deletions in 40-50% of the cases, +12 in 15-20% of the cases; 11q22-23 deletions in 7-10% of the cases; 17p13 deletions 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; -: positive in <10% of the cases; pan-B markers include CD19; CD20; CD79a R = rearranged; slg: surface immunoglobulins; cylg: 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-; slg+ 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 μm, i.e. < two red blood cells); atypical morphology: 10-55% of the lymphocytes are larger than 14 μm 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-; slg+ 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-; slg+ 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\(17p\) \(p53ID: 88> gene involved\) \(<5% of the cases\): Morphology consistent with CLL/PL Advanced disease; Refractoriness to purine analogs; Unfavourable prognosis CYTOGENETICS \(involved, mainly in the MTC and mTC1\)\(<5% of the cases\): 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+/-; slg+ 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 [BCL1ID: 36>](#)) [CYTOGENETICS](#)
[\(20-40% of cases\) with or without +3](#)

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