

Classification of B-cell chronic lymphoproliferative disorders (CLD): cytogenetic entities, immunophenotype and clinical features

Antonio Cuneo

Dipartimento di Scienze Biomediche - Sezione di Ematologia
 Università di Ferrara - Via Savonarola, 9 - 44100 FERRARA - ITALY
 tel. int+39.0532.236978; fax: int+39.0532.212142; e-mail sse@dns.unife.it
 February 2000

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. In this table 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 table dealing with NHL

Disease	Putative cell of origin and immunophenotype	Cytogenetic entities	Corresponding cytologic and clinical features
Chronic lymphocytic leukemia	CD5+ B cell that has encountered the antigen and harbours hypermutated IgV genes CD5+; CD23+; CD38+/-; CD22 weak+; FMC7-; slg+ weak	del(13q) (10-15% of the cases ¹)	Typical morphology ² ; indolent disease; favourable prognosis if present as the sole change
	CD5+ virgin recirculating B-cell with germline IgV genes CD5+; CD23+; CD38-/+; CD22 weak+; FMC7-; slg+ weak ³	+12 (10-15% of the cases ¹)	Frequent atypical morphology Relatively indolent disease Unfavourable prognosis as compared with other "single" chromosome aberrations, but not against complex karyotypes, 11q- or 17p-.
	CD5+ recirculating B-cell CD5+; CD23+; CD22 weak+; FMC7-; slg+ weak ³	11q22-23 deletion (ATM gene involved) (5-6% of the cases ¹)	Usually typical morphology with karyotype instability Relatively aggressive disease, with development of multiple adenopathies Unfavourable prognosis

		del(17p) (gene involved) (<5% of the cases ¹)	Morphology consistent with CLL/PL Advanced disease Refractoriness to purine analogs Unfavourable prognosis
		t(11;14)(q13;q32) (BCL1 BCL1 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
Prolymphocytic leukemia (PLL)	Peripheral B-lymphocyte that has encountered the antigen and harbours hypermutated IgV genes	t(11;14)(q13;q32) (BCL1 involved in the MTC and mTC1)	Rare and aggressive disease with a majority of relatively large lymphocytes with round nucleus and a prominent central nucleolus
Splenic lymphoma with villous lymphocytes	Marginal zone lymphocytes harbouring hypermutated IgV genes Pan-B+; CD5-/+; CD23-/+; CD11c+/-; CD25-/+; FMC7+/-; slg+ bright	t(11;14)(q13;q32) (20% of the cases) (breaks outside the MTC and mTC1 of BCL1 BCL1) 7q22-31 deletion 7q22-31 deletion (20-40% of cases) with or without +3	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

Legend : +: 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.

Comments:

1. The incidence for each of these chromosome lesions 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.
2. 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.
3. Approximately 70% of CLLs have the classical phenotype here summarized; the remaining cases show one or more deviations, which occur more frequently in morphologically atypical cases. These phenotype deviations include bright slg expression, FMC7+, CD23-, CD22 bright+. The entity of CLL/PL with t(11;14) usually, but not invariably, showed a consistently

overlapping phenotype with mantle cell lymphoma: these cases may represent the leukemic counterpart of a spectrum of neoplasias of follicle mantle lineage

References

1. Bennett JM, Catovsky D, Daniel MT, Flandrin G, Galton DAG, Gralnack HR, Sultan C. The French-American-British (FAB) Cooperative Group: Proposals for the classification of chronic (mature) B and T lymphoid leukemias. *J Clin Pathol* 1989; 42: 567-584. [Medline](#)
2. Bigoni R, Cuneo A, Roberti MG, Bardi A, Rigolin GM, Scapoli GL, Spanedda R, Negrini M, Bullrich F, Veronese ML, Croce CM, Castoldi GL: Chromosome aberrations in chronic lymphocytic leukemia mixed-cell type: A cytogenetic and interphase cytogenetic study. *Leukemia* 1997; 11:1933-1940 [Medline](#)
3. Cuneo, A., Bigoni, R., Negrini, M., Bullrich, F., Veronese, M.L., Roberti, M.G., Bardi, A., Rigolin, G.M., Cavazzini, P.L., Croce, C.M., Castoldi, G.L. (1997) Cytogenetic and interphase cytogenetic characterization of atypical chronic lymphocytic leukemia carrying BCL1 translocation. *Cancer Res* 1997; 57: 1144-1150. [Medline](#)
4. Hernandez JM, Mecucci C, Criel A, Meeus P, Michaux L, Van Hoof A, Verhoef G, Louwagie A, Scheiff JM, Michaux JL, Boogaerts M, Van Den Berghe H. Cytogenetic analysis of B-cell chronic lymphoid leukemias classified according to morphologic and immunophenotypic (FAB) criteria. *Leukemia* 1995; 9: 2140-2147. [Medline](#)
5. Juliusson G, Oscier DG, Fitchett M, Ross FM, Stockdill G, Mackie MJ, Parker A, Castoldi GL, Cuneo, Knuutila S, Elonen E, Gahrton G:
6. Prognostic subgroups in B-cell chronic lymphocytic leukemia defined by specific chromosomal abnormalities. *N Engl J Med* 1990; 323: 720-724. [Medline](#)
7. Naylor M, Capra JD. Mutational status of Ig VH genes provides clinically valuable information in B-cell chronic lymphocytic leukemia. *Blood* 1999; 94: 1837-1839. [Medline](#)
8. Stankovic T, Weber P, Stewart G, Bedenham T, Murray J, Byrd PJ, Moss PAH, Taylor AMR. Inactivation of ataxia telangiectasia mutated gene in B-cell chronic lymphocytic leukaemia. *Lancet* 1999; 353:26-29. [Medline](#)
9. Doehner H, Fisher K, Bentz M, Hansen K, Benner A, Cabot G, Diehl D, Schlenk R, Coy J, Stilgenbauer S, Volkmann M, Galle PR, Poustka A, Hustin W, Lichter P. p53 gene deletion predicts for poor survival and non-response to therapy with purine analogs in chronic B-cell leukemias. *Blood* 1995; 85: 1580-1589.
10. Doehner H, Stilgenbauer S, James MR, Benner A, Weilguni T, Bentz M, Fischer K, Hustin W, Lichter P. 11q deletions define a new subset of B-cell chronic lymphocytic leukemia characterized by extensive nodal involvement and inferior prognosis. *Blood* 1997; 89: 2516-2522.

Contributor(s)

Written 02- Antonio Cuneo
2000

Citation

This paper should be referenced as such :

Cuneo A . Classification of B-cell chronic lymphoproliferative disorders (CLD): cytogenetic entities, immunophenotype and clinical features. Atlas Genet Cytogenet Oncol Haematol. February 2000 .

URL : <http://AtlasGeneticsOncology.org/Deep/BCLDclassifID20013.html>

© *Atlas of Genetics and Cytogenetics in Oncology and Haematology*
