

Diffuse large cell lymphoma

Clinics and Pathology

Disease	diffuse large cell lymphoma (DLCL) includes centroblastic lymphoma, B-cell immunoblastic lymphoma and B-cell large cell anaplastic lymphoma in the Kiel classification; this neoplasia may present as a de novo condition or it may derive from the transformation of follicle centre cell lymphoma or, less frequently, of marginal zone lymphoma
Phenotype / cell stem origin	the tumor cells are pan-B+ and CD45+; CD5 and CD10 are positive in a minority of cases; positivity for surface Ig is found in the majority of cases, a minority of which also show intracytoplasmic Ig; some cases of the anaplastic subtype may be CD30+; usually, BCL6 is positive in cases with predominant centroblastic morphology, whereas syndecan-1 (CD138) tests positive in the immunoblastic variant; the putative normal cellular counterparts are cells of follicle / post follicle centre origin that have encountered the antigen and harbour somatic hypermutations of the Ig-gene variable region
Pathology	the cells are large, with vesicular nuclei at least twice the size of the nucleus of a small lymphocyte; there is a mixture of cells resembling centroblasts and immunoblasts; in rarer cases the cells are morphologically indistinguishable from those seen in anaplastic lymphoma of T- or null cell type

Genetics

the large majority of cases show clonal cytogenetic lesions; some of these changes are associated with a known primary genetic defect responsible for lymphomagenesis, whereas a plethora of additional changes may be involved in tumor progression.

most studies failed to establish the prognostic predictivity for any primary chromosome defect, whereas there is evidence that several secondary aberrations may affect prognosis.

Cytogenetics

Cytogenetics primary changes:

Morphological [t\(14;18\)\(q32;q21\)](#) / [BCL2](#)-rearrangement: this molecular cytogenetic defect is found in approximately 15-25% of the cases, many of which are thought to derive from the transformation of an antecedent follicle centre cell lymphoma; in virtually all cases additional cytogenetic defects are present, including 17p13/[p53](#) lesions; this balanced translocation can be demonstrated by conventional cytogenetics, by FISH and by molecular genetic methods. including southern blotting and PCR: the latter method is

useful for the monitoring of minimal residual disease.

[t\(3;V\)\(q27;V\) / BCL6](#)-rearrangement: chromosome translocations involving the 3q27 band with a number of partner chromosomes ([14q32](#), [2p11](#), [22q11](#), [4p11](#), 6p21, 11q23) are found in 5-10% of the cases by cytogenetic analysis, but the incidence of BCL6 rearrangement may reach 20-30% of the cases when investigated by southern blotting; there is not an absolute correlation between rearrangement of the 3q27 band and BCL6 involvement; cryptic BCL6 rearrangements were demonstrated by FISH, consisting of an insertion of IgH sequences within the regulatory portion of the BCL6 gene

[t\(8;14\)\(q24;q32\) / MYC](#) rearrangements: this aberration is found by cytogenetic or molecular genetic methods in 7-10% of the cases; probes for FISH detection of myc rearrangements were also tested successfully; an association with the centroblastic variant of DLCL was proposed.

Additional anomalies

secondary anomalies:

trisomies of chromosomes [3](#), 5, 7, 11, [12](#), [18](#) and X are usually encountered in >10% of the cases.

the most frequent monosomies include -13, -14, -15.

gains of 1q and 6p were reported in more than 10% of the cases.

frequently occurring deletions involve 1p, 6q, 7q32-ter, 8p, 9p, 11q, 17p.

the most frequent breakpoints are clustered in the following regions: 1cen-p13; 1p34-36; 3q21-22; 3q27-29; 6q12-16; 6q21-25; 7q32, 9cen-p21; 17cen-p12.

there are reports suggesting that an inferior prognosis may be associated with 1q21-23 breaks, with 1q23-32 duplications, with 6q21-25 breaks and with 11q22-23 deletion; complex karyotype may have an adverse impact on prognosis.

Bibliography

Cytogenetic analysis of 434 consecutively ascertained specimens of non-Hodgkin's lymphoma: clinical correlations.

Offitt K, Wong G, Philippa DA, Tao Y, Chaganti RSK.
Blood 1991; 77: 1508-1515.

A revised European-American classification of lymphoid neoplasms: a proposal from the international lymphoma study group.

Harris NL, Jaffe ES, Stein H, Banks PM, Chan JKC, Cleary ML, Delsol G, De Wolf-Peeters C, Falini B, Gatter KC, Grogan TM, Isaacson PG, Knowles DM, Mason DY, Muller-Hermelink HK, Pileri SA, Piris MA, Ralfkiaer E, Warnke RA.
Blood 1994; 84: 1361.

Medline [8068936](#)

Rearrangement of BCL-6 gene as a prognostic marker in diffuse large-cell lymphoma.

Offitt K, Lo Coco F, Louie DC, Parsa NZ, Leung D, Portlock C, Ye BH, Lista F, Filippa DA, Rosenbaum A, Landanyi M, Jhanwar S, Offitt K, Lo Coco F, Louie DC, Parsa

NZ, Leung D, Portlock C, Ye BH, Lista F, Filippa DA, Rosenbaum A, Landanyi M, Jhanwar S, Dalla-Favera R, Chaganti RSK.
New Engl J Med 1994; 331: 74-80.

Involvement of BCL6 in chromosomal aberrations affecting band 3q27 in B-cell non-Hodgkin's lymphoma.

Chaganti SR, Chen W, Parsa NZ, Offitt K, Louie DC, Dalla Favera R, Chaganti RSK.
Genes Chromosom Cancer 1998; 23: 323-327.
Medline [9824205](#)

Deregulation of BCL6 in non-Hodgkin's lymphoma by insertion of IgH sequences in complex translocations involving band 3q27.

Chaganti SR, Pulivarthi HR, Chen W, Dyomin V, Jhanwar SC, Parsa NZ, Dalla Favera R, Chaganti RSK.
Genes Chromosom Cancer 1998; 23: 328-336.
Medline [9824206](#)

Application of fluorescence i situ hybridization for the detection of the Burkitt translocation t(8;14)(q24;q32) in B-cell lymphomas.

Siebert R, Matthiesen P, Harder S, Zhang Y, Borowski A, Zuhlke-Jenisch R, Metzke S, Joos S, Weber-Matthiesen K, Grote W, Schlegelberger B.
Blood 1998; 91: 984-990.
Medline [9446660](#)

Interphase FISH in chronic lymphoproliferative disorders and comparative genomic hybridization in the study of lymphomas.

Bentz M, Stilgenbauer S, Lichter P, Dohner H.
Haematologica 1999; 84: (EHA educational book) 102-106.

World Health Organization classification of neoplastic diseases of hematopoietic and lymphoid tissues: Report of the clinical advisory committee Airlie House, Virginia, Novembre 1997.

Harris NNL, Jaffe ES, Diebold J, Flandrin G, Muller-Hermelink HK, Vardiman J, Lister TA, Bloomfield CD.
J Clin Oncol 1999; 17: 3835-3849.
Medline [10577857](#)

Clinicopathogenetic significance of chromosomal abnormalities in patients with blastic peripheral B-cell lymphoma.

Schlegelberger B, Zwingers T, Harder T, Nowotny H, Siebert R, Vesely M, Bartels H, Sonnen R, Hopfinger G, Nader A, Ott G, Muller-Hermelink K, Feller A, Heinz R, for the Kiel-Wien-Lymphoma Study Group.
Blood 1999; 94: 3114-3120.
Medline [10556197](#)

Acquired deletion of the ataxia teleangiectasia (ATM) locus in B-cell non-Hodgkin's lymphoma: correlation with clinicobiologic features.

Cuneo, A., Bigoni, R., Rigolin, G.M., Roberti, M.G., Bardi, A., Minotto, C., Agostini, P., Campioni, D., Milani, R., Narducci, M.G., Sabbioni, S., Russo, G., Negrini, M., Castoldi, G.

J Clin Oncol, 2000, in press.

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