

Leukaemia Section

Mini Review

Diffuse large cell lymphoma

Antonio Cuneo, Gian Luigi Castoldi

Hematology Section, Department of Biomedical Sciences, University of Ferrara, Corso Giovecca 203, Ferrara, Italy (AC)

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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

Note

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 morphological

Primary changes:

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.

References

Offit K, Wong G, Filippa DA, Tao Y, Chaganti RS. Cytogenetic analysis of 434 consecutively ascertained specimens of non-Hodgkin's lymphoma: clinical correlations. *Blood*. 1991 Apr 1;77(7):1508-15

Offit K, Lo Coco F, Louie DC, Parsa NZ, Leung D, Portlock C, Ye BH, Lista F, Filippa DA, Rosenbaum A. Rearrangement of the bcl-6 gene as a prognostic marker in diffuse large-cell lymphoma. *N Engl J Med*. 1994 Jul 14;331(2):74-80

Tse KF, Morrow JK, Hughes NK, Gallicchio VS. Stromal cell lines derived from LP-BM5 murine leukemia virus-infected long-term bone marrow cultures impair hematopoiesis in vitro. *Blood*. 1994 Sep 1;84(5):1508-18

Chaganti SR, Chen W, Parsa N, Offit K, Louie DC, Dalla-Favera R, Chaganti RS. Involvement of BCL6 in chromosomal aberrations affecting band 3q27 in B-cell non-Hodgkin

lymphoma. *Genes Chromosomes Cancer*. 1998 Dec;23(4):323-7

Chaganti SR, Rao PH, Chen W, Dyomin V, Jhanwar SC, Parsa NZ, Dalla-Favera R, Chaganti RS. Deregulation of BCL6 in non-Hodgkin lymphoma by insertion of IGH sequences in complex translocations involving band 3q27. *Genes Chromosomes Cancer*. 1998 Dec;23(4):328-36

Siebert R, Matthiesen P, Harder S, Zhang Y, Borowski A, Zühlke-Jenisch R, Metzke S, Joos S, Weber-Matthiesen K, Grote W, Schlegelberger B. Application of interphase fluorescence in situ Hybridization for the detection of the Burkitt translocation t(8;14)(q24;q32) in B-cell lymphomas. *Blood*. 1998 Feb 1;91(3):984-90

Bentz M, Stilgenbauer S, Lichter P, Döhner H. Interphase FISH in chronic lymphoproliferative disorders and comparative genomic hybridisation in the study of lymphomas. *Haematologica*. 1999 Jun;84 Suppl EHA-4:102-6

Harris NL, Jaffe ES, Diebold J, Flandrin G, Muller-Hermelink HK, Vardiman J, Lister TA, Bloomfield CD. World Health Organization classification of neoplastic diseases of the hematopoietic and lymphoid tissues: report of the Clinical Advisory Committee meeting-Airlie House, Virginia, November 1997. *J Clin Oncol*. 1999 Dec;17(12):3835-49

Schlegelberger B, Zwingers T, Harder L, Nowotny H, Siebert R, Vesely M, Bartels H, Sonnen R, Hopfinger G, Nader A, Ott G, Müller-Hermelink K, Feller A, Heinz R. Clinicopathogenetic significance of chromosomal abnormalities in patients with blastic peripheral B-cell lymphoma. Kiel-Wien-Lymphoma Study Group. *Blood*. 1999 Nov 1;94(9):3114-20

Cuneo A, Bigoni R, Rigolin GM, Roberti MG, Milani R, Bardi A, Minotto C, Agostini P, De Angeli C, Narducci MG, Sabbioni S, Russo G, Negrini M, Castoldi G. Acquired chromosome 11q deletion involving the ataxia teleangiectasia locus in B-cell non-Hodgkin's lymphoma: correlation with clinicobiologic features. *J Clin Oncol*. 2000 Jul;18(13):2607-14

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