Disease

Diffuse large cell lymphoma (DLCL) includes centroblastic lymphoma, \nB-cell immunoblastic lymphoma and B-cell large cell anaplastic lymphoma \nin the Kiel classification; this neoplasia may present as \nde novo condition or it may derive from the \ntransformation of follicle centre cell lymphoma or, less \nfrequently, of marginal zone lymphoma.

Phenotype/cell stem origin

The tumor cells are pan-B+ and CD45+; CD5 and \nCD10 are positive in a minority of cases; positivity for \nsurface Ig is found in the majority of cases, a minority of \nwhich also show intracytoplasmic Ig; some cases of \nanaplastic subtype may be CD30+; usually, BCL6 \nis positive in cases with predominant centroblastic \nmorphology, whereas syndecan-1 (CD138) tests \npositive in the immunoblastic variant; the putative \nnormal cellular counterparts are cells of follicle / post \nfollicle centre origin that have encountered the antigen \nand harbour somatic hypermutations of the Ig-gene \nvariable region.

Pathology

The cells are large, with vesicular nuclei at least twice \nthe size of the nucleus of a small lymphocyte; there is a mixture of cells resembling centroblasts and \nimmunoblasts; in rarer cases the cells are \nmorphologically indistinguishable from those seen in \nanaplastic 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 \nderive from the transformation of an antecedent follicle \ncentre cell lymphoma; in virtually all cases additional \ncytogenetic defects are present, including 17p13/p53 \nlesions; this balanced translocation can be \ndemonstrated by conventional cytogenetics, by FISH \nand by molecular genetic methods, including southern \nblotting and PCR; the latter method is useful for the \nmonitoring of minimal residual disease.
t(3;V)(q27;V) / BCL6-rearrangement: chromosome \ntranslocations involving the 3q27 band with a number of \npartner chromosomes (14q32, 2p11, 22q11, 4p11, \n6p21, 11q23 ) are found in 5-10% of the cases; by \ncytogenetic analysis, but the incidence of BCL6 \nrearrangement may reach 20-30% of the cases when \ninvestigated by southern blotting; there is not an \nabsolute correlation between rearrangement of the 3q27 \nband and BCL6 involvement; cryptic BCL6 \nrearrangements were demonstrated by FISH, consisting \nof an insertion of IgH sequences within the regulatory \nportion of the BCL6 gene.
t(8;14)(q24;q32) / MYC rearrangements: this \naberration is found by cytogenetic or molecular genetic \nmethods in 7-10% of the cases; probes for FISH

Phenotype/cell stem origin

The tumor cells are pan-B+ and CD45+; CD5 and \nCD10 are positive in a minority of cases; positivity for \nsurface Ig is found in the majority of cases, a minority of \nwhich also show intracytoplasmic Ig; some cases of \nanaplastic subtype may be CD30+; usually, BCL6 \nis positive in cases with predominant centroblastic \nmorphology, whereas syndecan-1 (CD138) tests \npositive in the immunoblastic variant; the putative \nnormal cellular counterparts are cells of follicle / post \nfollicle centre origin that have encountered the antigen \nand harbour somatic hypermutations of the Ig-gene \nvariable region.
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.