

Burkitt's lymphoma (BL)

Clinics and Pathology

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| Phenotype / cell stem origin | Pan-B antigens positive; TdT-, CD10+; CD5-; sIgM+. The cell of origin is a peripheral IgM+ memory B-cell (presence of somatic hypermutation of the Ig gene) |
| Epidemiology | Most common in children (1/3 of lymphomas). In adult it accounts for 3-4% of all lymphomas in western countries and it is frequently associated with immunodeficiency |
| Clinics | <p>There is an endemic variant, affecting africans, which primarily involves the jaws and other facial bones.</p> <p>The non-endemic variant may be associated with immunodeficiency states and usually presents with abdominal involvement (distal ileum, ciecum, mesentery). The disease is very aggressive and requires prompt treatment with appropriate regimens.</p> |
| Cytology | The blast cells in the peripheral blood and bone marrow display a basophilic cytoplasm with characteristic vacuolization, a picture indistinguishable from acute lymphoblastic leukemia (ALL) L3 of the FAB classification, which represents the leukemic counterpart of BL. |
| Pathology | <p>The lymphoma consists of a monomorphic infiltrate of the lymph node by medium-sized cells showing round nuclei with several nucleoli and basophilic cytoplasm. Numerous benign macrophages confer a histologic pattern referred to as ³starry sky². Involvement of the peripheral blood and bone marrow may occur.</p> <p>The related form ³Burkitt-like² lymphoma shows intermediate features between diffuse large cell lymphoma and BL and probably includes different disease entities. It was suggested by the WHO panel that only those cases with c-MYC rearrangement and/or a >99% proliferation fraction as demonstrated by Ki-67 positivity should be classified as Burkitt-like lymphoma</p> |
| Treatment | Aggressive regimens specifically designed for this lymphoma must be used |
| Evolution | Very rapid if untreated. Patients with limited disease and favourable prognostic features at presentation may rapidly show disease dissemination |
| Prognosis | If treated promptly with appropriate regimens the majority of patients can be cured |

Cytogenetics

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| Cytogenetics | The primary chromosome anomaly is the translocation |
| Morphological | t(8;14)(q24;q32) , found in 60-70% of the cases. Variant translocations having in common an 8q24 break, i.e the t(8;22)(q24;q11) and t(2;8)(p11;q24) occur in approximately 10-15% and 2-5% of the cases, respectively. A minority of cases may carry a duplication of chromosome 1, involving the 1q21-25 segment as the only detectable chromosome lesion |

In the Burkitt-like form there are at least 3 cytogenetic categories: one with an 8q24/c-MYC translocation, one with an 8q24 and [18q21/BCL2](#) translocation and another with ³miscellaneous² rearrangements, frequently including an 18q21 break

Probes

Conventional karyotyping is the method of choice for the detection of the 8q24 translocations occurring in BL.

There is variability in the location of the breakpoint at band 8q24, making the detection of c-MYC rearrangement (see below) difficult by molecular genetics. Southern blotting is the preferred method. In the endemic form the breakpoint in the Ig locus is usually located in the Ig heavy chain variable region, whereas in the nonendemic form the breakpoint falls in the Ig switch region.

Fluorescence in situ hybridization is of value in detecting the t(8;14) in interphase cells. Dual color FISH detection of the t(8;14) in interphase cells is possible by using cosmid clones spanning the c-MYC locus at 8q24 and a differently labelled IgH probe

Additional anomalies

Recurrent chromosome aberrations associated with the 8q24 translocations include 1q21<25 duplications, deletions of [6q11-14](#), [17p deletions](#) and [trisomy 12](#), +7, [+8](#) and [+18](#).

Genes involved and Proteins

Note

The t(8,14) and the variant t(8;22) and t(2;8) juxtapose [IgH](#) sequences and the [c-MYC](#) oncogene, bringing about its constitutional expression.

The 17p deletion may have a correlation with [p53](#) loss of function, determined by deletion of one allele and inactivating mutation of the remaining allele

Result of the chromosomal anomaly

Fusion Protein

Oncogenesis

Constitutive expression of c-MYC is crucial for the pathogenesis of BL, this protein being a key transcriptional regulator, controlling cell proliferation, differentiation and death. The deregulated expression of c-MYC, caused by the 8q24 translocations, is achieved through multiple mechanisms: a) juxtaposition to regulatory elements of the Ig loci, b) mutations in the c-MYC 5' regulatory regions and, c) aminoacid substitutions occurring in exon 2, making the c-MYC transactivation domain less susceptible to modulation

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