Classification of B-cell non-Hodgkin lymphomas (NHL)

Identity

Note

B-cell NHL include a number of clinicopathologic subsets of lymphoid neoplasms having heterogeneous features. This situation is reflected by variations in the classification systems that were proposed over the last decade. Cytogenetic findings were recognized to help defining a rationale biologic ground for the nosologic classification of lymphomas. An outlook of the salient cytogenetic entities in this spectrum of disorders is presented herein; a complete illustration of the cytogenetic profile of each disease is provided in specific cards. Unless otherwise specified the WHO classification system will be used.

Legend for immunophenotypes (below): +: 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; cyIg: cytoplasmic Ig; IgV genes: genes encoding for the variable portion of the Ig.

Clinics and Pathology

Disease

Small lymphocytic lymphoma (SLL)

Phenotype / cell stem origin

Histologic subset and Immunophenotype: Pan-B+; CD5+; CD23+; CD10-; slgM+ faint.

Putative cell of origin: CD5+ virgin B-cell with germline IgV genes (as was recently demonstrated to be the case with chronic lymphocytic leukemia, the leukemic counterpart of SLL, it is likely that part of the cases may derive from post-germinal centre quiescent B-cells that harbour hypermutated IgV genes)

Clinics

Indolent disease; leukemic involvement by lymphoid cells, including prolymphocytes and/or paraimmunoblasts Splenomegaly

Cytogenetics del(6)(q21-23) (20-30% of the cases)

Lymphoplasmacytic lymphoma

Phenotype / cell stem origin

Histologic subset and Immunophenotype: Pan-B+; CD5-; CD10-; cyIgM+

Putative cell of origin: Peripheral B-lymphocyte transforming into plasma cell with mutated IgV genes and ongoing mutations

Clinics

Indolent low-grade disease, with possible clinical and/or histologic
Cytogenetics  \( t(9;14)(p13;q32) \) PAX5/IgH (50% of cases)

**Disease**  Follicle centre cell lymphoma

**Phenotype / cell stem origin**  Histologic subset and Immunophenotype: Pan-B+; CD10+/-; CD5-; slg+

Putative cell of origin: Centrocyes / centroblasts of germinal centre origin with somatic hypermutation of the IgV genes and ongoing mutations (antigen driven stimulation)

**Clinics**  Indolent. Advanced stages predominate.

Conflicting data as to the prognostic significance of the \( t(14;18)/BCL2 \)

**Cytogenetics**  \( t(14;18)(q32;q21) \) / BCL2 Rearr (70-80% of cases)

**Disease**  Diffuse large cell lymphoma

**Phenotype / cell stem origin**  Histologic subset and Immunophenotype: CD19+; CD22+; CD10-/+; Slg+

Putative cell of origin: Large transformed B-cells harbouring somatic hypermutation of the Ig genes (ongoing mutations in some cases)

**Clinics**  Usually aggressive

Immunoblastic lymphoma (Kiel classification) do worse than centroblastic lymphomas

No convincing demonstration that any "primary" cytogenetic / molecular defect has prognostic significance; complex karyotype confers a shorter survival

**Cytogenetics**  \( t(14;18) \) and p53 mutations (20% of the cases)

\( t(3;V)(q27;V)/BCL6 \) Rearr (6-30% of cases (% variations depending on detection methods: molecular genetics and FISH more sensitive that conventional cytogenetics))

or variants c-MYC Rearr (7-10% of cases)

**Disease**  Burkitt's lymphoma

**Phenotype / cell stem origin**  Histologic subset and Immunophenotype: Pan-B+; TdT-; CD10+; CD5-; slgM+

Putative cell of origin: Peripheral B-cells that have encountered the antigen and harbour somatic hypermutation of the Ig genes

**Clinics**  Extremely aggressive disease

Specific treatment mandatory

**Cytogenetics**  \( t(8;14)(q24;q32) \) ID1050> or variants / R earr (80% of the cases)

GENES

**Disease**  Burkitt-like lymphoma

**Phenotype / cell stem origin**  Histologic subset and Immunophenotype: Pan-B+; TdT-; CD10-/+

Putative cell of origin: Peripheral B-cells that have encountered the
antigen

Clinics Aggressive disease
Cases with dual 8;14 and 14;18 translocations have a worse
goal (data requiring confirmation -1 study only)

Cytogenetics t(8;14) or variants (25% of cases)
 t(8;14)+ t(14;18) (30% of cases)

Disease Mantle cell lymphoma
Phenotype / Histologic subset and Immunophenotype: Pan-B +; CD5+; CD23-;
cell stem CD10-/+; slgM+ bright
origin Putative cell of origin: CD5+ B-cells of the follicle mantle having
germline IgV gene sequences

Clinics Advanced stages predominate
Response to chemotherapy often unsatisfactory
Short survival
Complex karyotype carries an unfavourable prognostic significance

Cytogenetics t(11;14)(q13;q32) / BCL1 Rearr (50-90%) (molecular genetic
methods have limited application due to variability of breakpoints; FISH
is the most sensitive technique)

Disease Marginal zone B-cell lymphoma (MZBCL)
Phenotype / Histologic subset and Immunophenotype: pan-B+; CD5-/+; CD10-;
cell stem CD23-; CD11c+/−; cylg + (40% of the cells), slgM+ bright; slgD-)
origin Putative cell of origin: Marginal zone lymphocytes harbouring
hypermutated IgV genes

Cytogenetics t(11;18)(q21;q21) ID: 2022> / P12 / MLT fusion (30-50% of the low-
grade MALT): Extra-nodal low-grade MALT lymphoma; indolent
disease
 t(1;14)(p21;q32): Extra-nodal MALT lymphoma
del(7)(q22-31) (40% of the cases): Splenic MZBCL
/+3q (30-70% of the cases): Nodal, extra-nodal and splenic MZBCL

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