Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

Leukaemia Section

Mini Review

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

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Published in Atlas Database: February 2000

Online updated version : http://AtlasGeneticsOncology.org/Anomalies/BNHLClassifID2067.html
DOI: 10.4267/2042/37588

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; sIg: 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-; sIgM+ 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).

Disease

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 progression.

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-; sIg+. Putative cell of origin: Centrocytes / 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-/+; SIg+.
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-; sIgM+.
Putative cell of origin: Peripheral B-cells that have encountered the antigen and harbours somatic hypermutation of the Ig genes.

Clinics

Extremely aggressive disease.
Specific treatment mandatory.

Cytogenetics

Or variants / c-MYC R earr (80% of the cases).

Disease

Burkitt-like lymphoma

Phenotype/cell stem origin

Histologic subset and Immunophenotype: Pan-B+; TdT-; CD10-/+ CD5-; sIg+.
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 outcome (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/cell stem origin

Histologic subset and Immunophenotype: Pan-B +; CD5+; CD23-; CD10-/+; sIgM+ bright.
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/cell stem origin

Histologic subset and Immunophenotype: pan-B+; CD5-/+; CD10-; CD23-; CD11c+/-; cyIg + (40% of the cells), sIgM+ bright; sIgD-).
Putative cell of origin: Marginal zone lymphocytes harbouring hypermutated IgV genes.

Cytogenetics

t(11;18)(q21;q21) *PI2*/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.
+3/+3q (30-70% of the cases): Nodal, extra-nodal and splenic MZBCL.

References

Offit K, Parsa NZ, Filippa D, Jhanwar SC, Chaganti RS. t(9;14)(p13;q32) denotes a subset of low-grade non-Hodgkin's lymphoma with plasmacytoid differentiation. Blood. 1992 Nov 15;80(10):2594-9

Tilly H, Rossi A, Stamatoullas A, Lenormand B, Bigorgne C, Kunlin A, Monconduit M, Bastard C. Prognostic value of chromosomal abnormalities in follicular lymphoma. Blood. 1994 Aug 15;84(4):1043-9

Kramer MH, Hermans J, Wijburg E, Philippo K, Geelen E, van Krieken JH, de Jong D, Maartense E, Schuuring E, Kluin PM. Clinical relevance of BCL2, BCL6, and MYC rearrangements in

diffuse large B-cell lymphoma. Blood. 1998 Nov 1;92(9):3152-62

Cuneo A, Bigoni R, Rigolin GM, Roberti MG, Bardi A, Piva N, Milani R, Bullrich F, Veronese ML, Croce C, Birg F, Döhner H, Hagemeijer A, Castoldi G. Cytogenetic profile of lymphoma of follicle mantle lineage: correlation with clinicobiologic features. Blood. 1999 Feb 15;93(4):1372-80

Dierlamm J, Baens M, Wlodarska I, Stefanova-Ouzounova M, Hernandez JM, Hossfeld DK, De Wolf-Peeters C, Hagemeijer A, Van den Berghe H, Marynen P. The apoptosis inhibitor gene API2 and a novel 18q gene, MLT, are recurrently rearranged in the t(11;18)(q21;q21) associated with mucosa-associated lymphoid tissue lymphomas. Blood. 1999 Jun 1;93(11):3601-9

Küppers R, Klein U, Hansmann ML, Rajewsky K. Cellular origin of human B-cell lymphomas. N Engl J Med. 1999 Nov 11;341(20):1520-9

López-Guillermo A, Cabanillas F, McDonnell TI, McLaughlin P, Smith T, Pugh W, Hagemeister F, Rodríguez MA, Romaguera JE, Younes A, Sarris AH, Preti HA, Lee MS. Correlation of bcl-2 rearrangement with clinical characteristics and outcome in indolent follicular lymphoma. Blood. 1999 May 1;93(9):3081-7

Macpherson N, Lesack D, Klasa R, Horsman D, Connors JM, Barnett M, Gascoyne RD. Small noncleaved, non-Burkitt's (Burkit-Like) lymphoma: cytogenetics predict outcome and reflect clinical presentation. J Clin Oncol. 1999 May;17(5):1558-67

Panayiotidis P, Kotsi P. Genetics of small lymphocyte disorders. Semin Hematol. 1999 Apr;36(2):171-7

Richardson MA. Research of complementary/alternative medicine therapies in oncology: promising but challenging. J Clin Oncol. 1999 Nov;17(11 Suppl):38-43

Willis TG, Jadayel DM, Du MQ, Peng H, Perry AR, Abdul-Rauf M, Price H, Karran L, Majekodunmi O, Wlodarska I, Pan L, Crook T, Hamoudi R, Isaacson PG, Dyer MJ. Bcl10 is involved in t(1;14)(p22;q32) of MALT B cell lymphoma and mutated in multiple tumor types. Cell. 1999 Jan 8;96(1):35-45

This article should be referenced as such:

Cuneo A. Classification of B-cell non-Hodgkin lymphomas (NHL). Atlas Genet Cytogenet Oncol Haematol. 2000; 4(1):24-26.