Immunohistochemical classification of B cell neoplasms

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DIAGNOSTIC BRIEF

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In the new World Health Organisation (WHO) classification of haematological malignancies, immunophenotypical analysis is important in the subclassification of lymphomas.[1] In the past decade, many new antibodies have become available that can be used on routinely fixed, paraffin wax embedded tissue sections.[2 3] At present, it is possible to make a correct subclassification of B cell lymphomas in most cases using a relatively restricted set of markers. However, in some cases it may be difficult to differentiate a benign B cell response from a malignant B cell proliferation. In these cases, clonality analysis based on the presence of monoclonal immunoglobulin rearrangements is indicated. Moreover, the detection of specific translocations involving the c-myc, bcl-2, or cyclin D1 locus by molecular analysis may be required to make a definite diagnosis of Burkitt's(like), follicular, or mantle cell lymphoma, respectively.

Whenever an immunodeficiency associated lymphoproliferative disorder is considered, RNA in situ hybridisation detecting the abundantly transcribed Epstein-Barr virus (EBV) encoded RNAs is indicated, because most of these lymphoproliferative disorders are EBV positive. EBV encoded latent membrane protein 1 is not always detectable in these lymphoproliferative disorders and is thus unreliable for the detection of EBV. In addition, clonality analysis may be indicated in these lymphoproliferative disorders because polyclonal proliferations usually respond to a decrease in immunosuppressive treatment. However, monoclonal proliferations may also respond to a reduction in immune suppression.[1]

In table 1, the most discriminating markers are depicted in relation to the most frequently occurring entities, as recognised by the WHO classification. It is important to note that there are many exceptions to the patterns depicted in table 1, so that immunohistochemical results need to be correlated with morphology and clinical findings. In addition, the demonstration of monotypic light chain immunoglobulin expression can be helpful in the distinction from reactive B cell infiltrates. The detection of heavy chain class expression can be helpful in subclassification, but is not used for routine diagnostic purposes in our laboratory.

Table 1 Interpretation of immunohistochemistry

	CD20	CD79a	CD5	CD10	CD11c	CD23	Cyclin D1	Bcl2	Bcl6	TdT	Characteristic feature(s)
Predominantly small cell lymphomas											
Precursor B lymphoblastic leukaemia	–	+	–	+	–	–	–	+/–	–	+	Monotonous appearance, finely dispersed chromatin pattern
CLL/SLL	+	+	+	–	–	+	–	+	–	–	Clumped chromatin, low mitotic rate
B cell prolymphocytic leukaemia	+	+	–/+	–	–	–	–	+	–	–	High lymphocyte count (>100×10⁹/l)
Lymphoplasmacytic lymphoma	+	+	–	–	–	–	–	+	–	–	Intranuclear inclusion (Dutcher) bodies, monoclonal IgM paraprotein
Splenic marginal zone lymphoma	+	+	–	–	–	–	–	+	–	–	Often presence of villous lymphocytes in the blood
Hairy cell leukaemia*	+	+	+	–	+		–	+	–	–	Increase of reticulin fibres in the bone marrow
Plasma cell myeloma/extraosseous plasmacytoma†	+/–	+	–	–	–	–	–/+	+	–	–	Monotypic cytoplasmic expression of either κ or λ immunoglobulin light chain
Nodal and extranodal marginal zone lymphoma	+	+	–	–	+/–	–	–	+	–	–	Perifollicular growth pattern. In MALT presence of lymphoepithelial lesions
Follicular lymphoma	+	+	–	+	–	–	–	+	+	–	Aggregates of CD21 positive follicular dendritic cells
Mantle cell lymphoma	+	+	+	–	–	–	+	+	–	–	Presence of epithelioid (pink) histiocytes
Predominantly large cell lymphomas											
Diffuse large B cell lymphoma‡	+	+	–	+/–	–	–	–	+/–	+/–	–	Nuclear size > normal macrophage nucleus
Burkitt's lymphoma§	+	+	–	+	–	–	–	–	+	–	Starry sky appearance, cohesive growth pattern

*No specific marker exists for distinguishing hairy cell leukaemia from other B cell leukaemias. Apart from CD11c, the expression of tartrate resistant acid phosphatase and CD103 (frozen material) are helpful, together with the characteristic morphological features. †Plasmacytomas are positive for CD138, which is a sensitive, although not specific, marker for plasma cells. ‡These include immune deficiency related lymphoproliferative disorders. However, these disorders may show decreased CD79a and/or CD20 expression, and may show prominent plasmacytic differentiation. §Burkitt's lymphoma cannot always be distinguished from diffuse large B cell lymphoma based on the marker profile. The Ki-67 antibody can be helpful to determine whether all neoplastic cells are proliferating, supporting the diagnosis of Burkitt's lymphoma.
CLL/SLL, chronic lymphocytic leukaemia/small lymphocytic leukaemia; MALT, mucosa associated lymphoid tissue; TdT, terminal deoxynucleotidyl transferase; +, positive as a rule; –, negative as a rule; +/–, usually positive, sometimes negative; –/+, usually negative, sometimes positive.

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