Immunohistochemical classification of B cell neoplasms

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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.

REFERENCES


Table 1 Interpretation of immunohistochemistry

<table>
<thead>
<tr>
<th>Predominantly small cell lymphomas</th>
<th>CD20</th>
<th>CD5</th>
<th>CD10</th>
<th>Bcl2</th>
<th>Bcl6</th>
<th>CD11c</th>
<th>CD23</th>
<th>Cyclin D1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predominantly large cell lymphomas</td>
<td>CD20</td>
<td>CD5</td>
<td>CD10</td>
<td>Bcl2</td>
<td>Bcl6</td>
<td>CD11c</td>
<td>CD23</td>
<td>Cyclin D1</td>
</tr>
</tbody>
</table>

*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 immunocomplex mediated and plasma cell myeloma. The diagnosis of the 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.