INTRODUCTION

Histologically low grade (small cell predominant) B cell lymphomas are the most common broad group of non-Hodgkin’s lymphomas encountered by general histopathologists. With advances in clinical management it is increasingly important to correctly subclassify these lymphomas to both direct appropriate therapy and accurately assess prognosis. Improved antigen retrieval and widening of the panel of antigens that can be detected in routinely processed and paraffin embedded surgical biopsy material have greatly facilitated the assessment of lymphomatous infiltrates. Careful histological evaluation combined with appropriate immunophenotyping should allow the correct classification of these lymphomas in the majority of cases (Table 1). This article attempts to highlight the common histological and immunophenotypic features that help in addressing particular diagnostic problems. The discussions reflect the common histological and immunophenotypic patterns and should not be considered to be exhaustive. Exceptions will occur both in the histological patterns and in the immunophenotype within each of the groups encountered and there may be overlap between the histological groups. In difficult or confusing cases the histological pattern is usually more reliable than the immunophenotypic data, which is frequently a more variable characteristic. In such cases a wide experience of haematopathology becomes important in optimal classification. As with all tumours it will not be possible to classify every case and the category ‘unclassified’ is acceptable in those cases.

FOLLICULAR HYPERPLASIA AND FOLLICULAR LYMPHOMA

Histology

Almost all follicle centre cell lymphomas have at least a small area with a follicular growth pattern. A small proportion will have a dominant diffuse area but pure diffuse follicle centre cell lymphomas are very rare (less than 5% of cases). In follicle centre cell lymphoma the follicle formation is present both in the cortex and in the medulla with effacement of the normal architecture. The neoplastic follicles have a relatively uniform shape and size compared to reactive follicles which have variable shape and size. The follicle centres in follicular lymphomas are usually poorly demarcated and the surrounding mantle is frequently narrow and may be partially or completely absent. In follicular hyperplasia the follicle centre has a sharp demarcation from a normally developed mantle. The germinal centres of follicular lymphomas show an absence of the usual zoned pattern seen in reactive follicle centres and there are few intrafollicular macrophages (Fig. 1A). In follicle centre cell lymphoma there is a diffuse admixture of centrocytes and centro-
blasts with the former usually in the majority (Fig. 1B) while a reactive germinal centre comprises a dark zone containing numerous centroblasts with an upper light zone containing fewer centroblasts and more centrocytes. Mitoses are much more frequent in reactive compared to neoplastic follicle centres.

The inter-follicular zone in these lymphomas contains a population of follicle centre cells related to those within the follicles and there may occasionally be monotypic plasma cells. In reactive follicular hyperplasia the inter-follicular zone contains a heterogeneous mixture of cells including polyclonal plasma cells, T cells and some transformed B immunoblasts. The sinuses in reactive nodes are patent and may show sinus histiocytosis.

**Immunophenotype**

Generally, the immunophenotype of the cells of follicular lymphoma mimics that of the normal germinal centre. Thus follicular lymphoma cells are CD10 positive in 60–80% of cases and they are generally negative for CD5 and CD43. The use of anti-CD10 antibodies may also highlight the inter-follicular component that is frequently encountered in cases of follicle centre cell lymphoma (Fig. 1C) while no interfollicular CD10 positive centrocytes or centroblasts are seen in reactive nodes. Bcl-2 protein expression is helpful in the distinction between reactive and neoplastic germinal centres. Normal germinal centre B cells do not express bcl-2 protein (although the intrafollicular T cells are bcl-2 protein positive) while neoplastic follicle centre cells frequently express this protein. In many cases the expression of the protein is strong (frequently stronger than the surrounding mantle and T cell populations) but in some cases the expression is very weak and only careful examination of the cells (particularly the centroblasts as these cannot be confused with intrafollicular T cells) confirms a positive signal. Another marker that is helpful in the distinction between reactive and neoplastic follicle centres is an indicator of proliferation such as Ki-67 or MiB1. Reactive germinal centres show high proliferation and the use of these markers highlights the zoned pattern of the follicle centres. On the other hand, neoplastic follicle centres generally show low proliferation.

**Table 1** Commonest immunophenotype of the different low grade B cell lymphomas

<table>
<thead>
<tr>
<th>CD20</th>
<th>CD79a</th>
<th>CD10</th>
<th>CD23</th>
<th>CD5</th>
<th>CD43</th>
<th>DBA44</th>
<th>bcl-2 protein</th>
<th>CyclinD1</th>
<th>TdT</th>
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**Figure 1** (A) Reactive lymphoid follicle showing classical zones pattern with many macrophages and good distinction between follicle centre and mantle. (B) Follicle centre cell lymphoma with no zoning of the follicle, few macrophages and poor demarcation between neoplastic follicle centre and attenuated mantle. (C) CD10 staining in follicular lymphoma can help to highlight interfollicular neoplastic cells.
It should be noted that not all cases of follicle centre cell lymphoma express bcl-2 protein. Cases that are bcl-2 protein negative frequently show high proliferation and will therefore mimic reactive hyperplasia. As with all lymphoid proliferations clonality is the gold standard for the distinction between neoplastic and reactive lymphoid populations. Thus high quality staining for immunoglobulin light chain is essential in equivocal cases.

**PRACTICE POINTS**

Features favouring the diagnosis of follicle centre cell lymphoma over follicular hyperplasia:

**Histology**
- Follicles in cortex and medulla
- Uniform shape and size of follicles
- Mantle attenuated/absent
- Poor demarcation between follicle centre and surrounding cells
- Follicles with no zoned pattern, few macrophages and few mitoses

**Immunophenotype**
- Bcl-2 protein expression in follicle centre cell B cells
- Low proliferation
- CD10 positive follicle centre cells in interfollicular areas
- Immunoglobulin light chain restriction

**SMALL LYMPHOCYTIC LYMPHOMA/B-CHRONIC LYMPHOCYTIC LYMPHOMA AND MANTLE CELL LYMPHOMA**

**Histology**

It is important to distinguish mantle cell lymphoma (MCL) from small lymphocytic lymphoma (SLL), as MCL has a much poorer prognosis.9 Both SLL (or nodal involvement by B-chronic lymphocytic leukaemia, which is morphologically identical) and conventional MCL share superficially similar low and high power appearances. MCL may have a nodular appearance reflecting colonised follicles but most commonly has a diffuse pattern. SLL is characterised by numerous pale areas composed of the large, proliferating cells of SLL. These may give a pseudonodular appearance mimicking the colonised germinal centres seen in MCL. Usually, however, the colonised germinal centres in MCL contain large numbers of small mantle cells, in contrast to the pallor of the SLL proliferation centres. Approximately 10% of SLL cases lack proliferation centres, thus having a diffuse pattern similar to most cases of MCL.10 Even in these diffuse SLL cases, paraimmunoblasts and prolymphocytes should be identifiable randomly scattered amongst the predominating small cell population. In contrast, MCL comprises a pure small cell population.

At high power and in cytological preparations, SLL and MCL cells may be quite similar. SLL cells usually have very condensed or clumped chromatin and have very regular nuclei. MCL cells have somewhat more dispersed nuclear chromatin and more irregular nuclei (Fig. 2A). However, morphological overlap is considerable. In cases of SLL prolymphocytes (small cells with vesicular nuclei and distinct nucleoli) and paraimmunoblasts (large cells with copious cytoplasm and vesicular nuclei resembling immunoblasts) can be identified (Fig. 2B). These cells are lacking in MCL, although care must be taken not to mistake residual centroblasts or follicular dendritic cells (FDCs) in colonised follicles for paraimmunoblasts.

**Immunophenotype**

Both SLL and MCL share an aberrant expression of CD5 and CD43 and are negative for CD10; CD23 helps distinguish these two entities as it is positive in SLL and negative in MCL. However, CD23 immunostaining is not entirely reliable in paraffin sections, as it is usually positive only within SLL proliferation centres and positivity may be difficult to distinguish from FDCs in residual germinal centres.11 In difficult cases, a CD21 im-

![Figure 2](image.png)

(A) Mantle cell lymphoma. There is a uniform population of small cells with irregular nuclear contour and finely dispersed chromatin. Large cells are absent. (B) Small lymphocytic lymphoma. Small cells predominate outside the proliferation centres. These have round regular nuclei with condensed chromatin including several dark chromocentres. Occasional paraimmunoblasts with prominent nucleoli are seen.
munostain should highlight a residual FDC network in the colonised follicles, whilst SLL proliferation centres lack FDCs. Flow cytometric analysis on peripheral blood, bone marrow aspirate or disaggregated cells from a lymph node is preferable: MCL characteristically is CD23 negative, FMC7 positive and shows intermediate to strong surface immunoglobulin expression, in contrast to SLL which is usually CD23 positive, FMC7 negative and shows weak surface immunoglobulin expression.

The t(11;14)(q13;q32) chromosomal translocation characteristic of MCL is lacking in SLL, and is a very useful feature in distinguishing these two entities. Although the proportion of MCL cases which have molecular lesions involving the cyclin D1 gene varies according to the detection method used, FISH analysis has detected this lesion in over 95% of cases. By immunohistochemistry, up to 70% of MCL cases express cyclin D1 protein. Cyclin D1 is not expressed in normal lymphocytes or in other lymphoproliferative disorders. Thus, cyclin D1 immunostaining may be useful in identifying a case as MCL, although if negative it does not exclude MCL.

**Immunophenotype**

A number of immunohistochemical features help distinguish blastoid MCL from LBL. Unlike B cell LBL, MCL coexpresses CD5 along with B cell markers and is TdT negative. If cyclin D1 is positive, it excludes LBL; a negative result does not exclude MCL, however (see above). One caveat is that MCL (and SLL) cells express CD5 at a weaker level than the intermixed reactive T cells. This expression should be carefully compared with the negative control slide to verify low-level expression rather than non-specific background. Proliferation markers (such as Ki67 or MiB1) usually mark a higher proportion of cells in LBL (90% or more) than blastoid MCL (in the range of 50%).

**Lymphoplasmacytoid lymphoma and other small B lymphoproliferative disorders**

**Histology**

Plasma cells may be present in many lymphoproliferative disorders, either as reactive elements or as a clonal component of the neoplasm. Lymphoplasmacytoid lymphoma (LPL) or immunocytoma is characterised by a mixed population of small lymphocytes resembling SLL cells, plasma cells, and characteristic intermediate forms termed lymphoplasmacytoid cells. These cells have either a lymphocyte-like nucleus accompanying a plasma cell-like cytoplasm, or a plasma cell-like nucleus accompanied by very scant, pale cytoplasm. Intranuclear immunoglobulin inclusions (Dutcher bodies) are common in lymphoplasmacytoid cells (Fig. 3), although these can also be seen in the plasma cells of multiple myeloma and even in reactive plasma cells. Mast cells are present in high numbers in most cases of LPL. However, this is not a specific criterion, as increased mast cells may be seen in a number of other types of lymphomas, particularly when they involve the bone marrow.

**Figure 3** Lymphoplasmacytoid lymphoma. There are small cells with nuclei resembling plasma cells. Some cells contain intranuclear inclusions (Dutcher bodies).
SLL with clonal plasma cells may resemble LPL. However, LPL lacks proliferation centres and conversely, SLL should have no or very few true lymphoplasmacytoid cells and Dutcher bodies are not seen. Morphologically marginal zone B cell lymphoma (MZL) usually has a prominent population of monocytoid cells with round or oval nuclei and moderate amounts of abundant pale cytoplasm, but these may be difficult to see in routine sections. Clinical factors are also helpful: a substantial proportion of LPL cases fall into the clinicopathological entity of Wädenstrom’s macroglobulinaemia (circulating IgM and hyperviscosity). By contrast, paraprotein is not as common in MZL. In mucosal sites, even lymphoma cases with a large number of lymphoplasmacytoid cells are probably considered as MZL/MALT rather than LPL.

Immunophenotype

Immunophenotypically, LPL is by definition CD5 negative and by flow cytometry shows strong surface immunoglobulin expression, in contrast to SLL. The morphologically mixed cell population in LPL is also characterised by ‘crossover’ immunoreactivity, whereby the plasma cells often express CD20 and the small lymphocytes are immunoreactive for VS38c, which normally does not mark lymphocytes. Occasionally the differential of a small cell myeloma may arise; in such cases, demonstration of IgM heavy chain on the neoplastic plasma cell population is helpful in favouring LPL, as less than 1% of myelomas express IgM. Also, myelomas will lack a significant CD20 positive cell population.

Amongst small B cell lymphomas, which are CD5 and CD10 negative, the main differential diagnosis is usually between LPL and MZL. Immunophenotypically, these are indistinguishable, and in fact are probably biologically related entities, both resembling very differentiated B cells.

LOW GRADE B CELL LYMPHOMA OF MUCOSA ASSOCIATED LYMPHOID TISSUE AND REACTIVE LYMPHOID INFILTRATES

Histology

The distinction between florid reactive lymphoid infiltrates at extranodal sites and low grade B cell lymphomas of mucosa associated lymphoid tissue (MALT) can be difficult and this is a problem most commonly encountered in the stomach. Crucial to the investigation of such infiltrates is the quantity and the quality of the material. Biopsy specimens should be as large as possible and crushed areas should only be interpreted with extreme caution. If there is a suspicion of a lymphomatous infiltrate it may be necessary to perform a second endoscopy with multiple biopsy samples and, where possible, the use of ‘jumbo’ forceps is recommended in these circumstances as these give material from the full thickness of the mucosa as well as the superficial parts of the submucosa.

In reactive gastritis associated with Helicobacter pylori (Hp) there are invariably lymphoid follicles. These usually have the characteristics of normal reactive germinal centres surrounded by a mantle zone. Outside the mantle there may be a marginal zone of lymphocytes with slightly more abundant cytoplasm and there is usually a moderately dense plasma cell infiltrate in the superficial lamina propria. As this lymphoid tissue constitutes acquired MALT there may be interaction of small B lymphocytes with glandular epithelium. In gastritis this takes the form of small groups (3–5) of cells without cytological atypia which infiltrate the epithelium without destruction of the glandular structure. In general the lymphocytic infiltrate (as opposed to the plasma cells) is confined to the immediate vicinity of the follicles. As the follicles are found in, or just above, the muscularis propria there is frequently disruption of this structure and there may be overspill of lymphocytes into the submucosa.

In gastric MALT lymphoma lymphoid follicles are also invariably present but in some cases they may be difficult to detect as they have been overrun by the neoplastic cells. As these lymphomas arise within the background of a reactive, usually Hp associated, gastritis there is also a reactive plasma cell population. Several features have been described that are considered to be highly associated with neoplastic infiltrates and these form the basis of morphological criteria for the diagnosis of MALT lymphoma. These may not be present in all biopsies nor are they all present in all cases and the absence of no one feature excludes the diagnosis of lymphoma. Two of the most important characteristics for the diagnosis of gastric MALT lymphoma are the cellular infiltrate and the presence of lymphoepithelial lesions. Generally the lymphoid infiltrate is more lymphocyte dominant than is seen in reactive gastritis with extension of the lymphocytes away from the immediate vicinity of the lymphoid follicles to become broad sheets and/or extensive infiltration around gland structures. The presence of cellular atypia and centrocyte-like cell morphology is also associated more with lymphoma than reactive infiltrates. There is invariably plasma cell differentiation in MALT lymphoma and this does not help distinguish reactive from neoplastic infiltrates but the detection of Dutcher bodies is more consistent with lymphoma than uncomplicated gastritis. Dutcher bodies, however, are only detected in a minority of cases of MALT lymphoma. Lymphoepithelial lesions are characteristic of MALT lymphomas at any site. They must be distinguished from isolated infiltration of glands by small groups of reactive lymphocytes and are strictly defined as infiltration and destruction of epithelial structures by large groups of lymphocytes which show cytological atypia (Fig. 4).

In MALT lymphomas at non-gastrointestinal sites the same morphological criteria hold for the distinction between reactive and neoplastic lymphoid infiltrates. A useful feature that raises the possibility of lymphoma in
sites such as the salivary gland and thyroid is the presence of an expanded marginal zone of large cells with clear cytoplasm which is seen between the mantle of the lymphoid follicle and the epithelial structure. This is frequently the earliest indication of an evolving lymphoma.22

Immunophenotype

Immunophenotypic studies can be difficult to interpret in small biopsy specimens such as those taken at endoscopy. Underlying structures can be highlighted by the use of antibodies against cytokeratin and follicular dendritic cells (FDCs). The former is very useful in highlighting the presence of lymphoepithelial lesions while detection of FDC related antigens (e.g. CD21) can demonstrate distorted networks which may not be histologically apparent but which indicate follicle centres that have been overrun by small lymphocytes.19 Use of anti-CD20 demonstrates the distribution of the B lymphocyte population in the absence of plasma cell staining and is useful in confirming the B cell nature of the intraepithelial lymphocyte component. Crucial to the distinction between reactive and neoplastic lymphoid infiltrates is the detection of immunoglobulin light chain restriction. Light chain staining is frequently difficult to interpret in small crushed gastric biopsies and this is compounded by the fact that the neoplastic population may be admixed with a coexistent reactive population. Reactive plasma cells are invariably present in cases of MALT lymphoma and these may mask the light chain restriction in the atypical lymphoid cells making close and detailed examination of these stains essential in the assessment of light chain expression. Some cases of MALT lymphoma (20–40%) express the antigen CD43.23 In lymphoid populations this antigen is associated with T cell phenotype and aberrant expression of the T cell related marker by a B cell population is highly suggestive of a neoplastic B cell infiltrate.

LOW GRADE B CELL LYMPHOMA OF MUCOSA ASSOCIATED LYMPHOID TISSUE, MANTLE CELL LYMPHOMA AND FOLLICLE CENTRE CELL LYMPHOMA

Histology

Each of these lymphomas may involve extranodal sites and may have a nodular growth pattern at low power. Follicle centre cell lymphoma may be difficult to distinguish from those cases of MALT lymphoma that show a high degree of follicular colonisation. The cellular composition of the infiltrate may be very similar as nucleolated transformed cells and centrocyte-like cells of MALT lymphoma resemble centroblasts and centrocytes respectively. Generally the MALT lymphomas have a more extensive extracellular component than follicle centre cell lymphoma. Lymphoepithelial lesions are certainly more frequently encountered in MALT lymphoma but identical structures may be encountered in follicle centre cell lymphoma (personal observations; Isaacson, personal communication).

MCL, like MALT lymphoma is commonly associated with a nodular growth pattern (Fig. 5 a and b). The cellular morphology of the cells of MCL can resemble centrocyte-like cells but the composition is more uniform and monotonous in mantle cell lymphoma (Fig. 2a) where there is usually an absence of transformed blastic cells and of plasma cells. Occasionally structures resembling lymphoepithelial lesions can be encountered in MCL and this is most commonly seen in the colon in cases of lymphomatous polyposis coli (personal observations).

Immunophenotype

The characteristic immunophenotypic profile of these three lymphomas can usually distinguish the entities with
confidence. Each express the B cell related antigens CD20 and CD79a and they all usually express bcl-2 protein. Follicle centre cell lymphoma is usually CD10 positive (60–80%) but negative for CD5 and CD43. These lymphomas commonly express bcl-6 protein and they are negative for cyclinD1. Mantle cell lymphomas are CD10 negative but usually express CD5 and CD43 and they are characteristically positive for cyclinD1 but negative for bcl-6 protein. MALT lymphomas do not normally express CD10. A small minority of cases of MALT lymphoma have been reported in the literature showing expression of CD5. It is possible that expression of this antigen in MALT lymphoma is associated with a more disseminated disease. A proportion of cases of MALT lymphoma (20–40%) express CD43. They are usually negative for bcl-6 protein and do not express cyclin D1.

**PRACTICE POINTS**

Immunophenotypic features favouring MALT lymphoma over other low grade B cell lymphomas:

- MALT lymphoma over mantle cell lymphoma
  - CD5 negative
  - CyclinD1 negative

- MALT lymphoma over follicle centre cell lymphoma
  - CD10 negative
  - CD43 positive
  - bcl-6 negative

**SPLENIC MARGINAL B CELL LYMPHOMA AND B SMALL LYMPHOCYTIC, MANTLE CELL AND FOLLICLE CENTRE CELL LYMPHOMAS IN THE SPLEEN**

**Histology**

Almost all low grade B cell lymphomas predominantly involve the white pulp and can have a marginal zone pattern of infiltration in the lymph node. Splenic marginal zone B cell lymphoma (SMZL) is characterised by predominantly white pulp infiltration based on pre-existing follicles. In most nodules the follicle centres are not apparent with the central portion of the nodule reduced to a small hyalinised area. In a few nodules there are preserved follicle centres with normal appearing follicle centre cells. The neoplastic infiltrate is composed of an inner zone of small lymphocytes with scanty cytoplasm (resembling, and initially mistaken for, mantle zone B cells) and an outer zone of cells with more abundant cytoplasm. The outer zone may contain plasma cells and invariably contains transformed blast cells. The red pulp may be diffusely involved but frequently contains nodules of neoplastic cells which are normally those found in the inner zone of the white pulp infiltrate. Sinusoidal infiltration may be prominent.

Follicle centre lymphomas rarely present with splenomegaly. They usually show expansion of the follicle centres which contain centroblasts and centrocytes. There may be a peripheral zone to the follicle centres which contain cells resembling marginal zone cells but there is no intervening mantle zone. In some cases there may be both a mantle and marginal zone around the neoplastic follicles.

Mantle cell lymphoma involving the spleen may show a mantle zone pattern around reactive germinal centres or may present solid nodules. There may be diffuse red pulp infiltration. There may be an outer zone of cells with a more marginal zone pattern which is a part of the neoplastic infiltrate. A useful distinction with SMZL is the absence of transformed blast cells within this region.

Infiltration of the spleen by B chronic lymphocytic lymphoma (B-CLL) gives characteristic nodules of small lymphocytes which may be accompanied by central collections of larger nucleolated cells with features of prolymphocytes and para-immunoblasts characteristic of proliferation centres. Red pulp infiltration is usually present.

**Immunophenotype**

Immunophenotypic studies can usually distinguish between the common small B cell lymphomas within the spleen. When problems arise these are usually associated with poor preservation and fixation of the spleen. In ideal circumstances the splenectomy specimen should be received in the laboratory as soon after removal from the patient as possible. The spleen should be weighed and measured in the normal way and carefully sliced.

**Figure 5** Low power showing similar nodular pattern in (a) MALT lymphoma and (b) mantle cell lymphoma.
Block sized tissue samples should be selected and fixed separately. This allows prompt and appropriate fixation of a tissue that normally has slow formalin penetration if left intact.

All small B cell lymphomas express pan-B cell antigens (CD20 and CD79a) and show immunoglobulin light chain restriction. SMZL is generally IgD positive and expression of CD10, CD5 or CD43 is not normally detected in parrain section.29 Residual follicle centres may be identified as they will be bcl-2 protein negative while the neoplastic SMZL cells are bcl-2 protein positive. Follicle centre cell lymphomas are usually CD10 positive and the follicle centres (which are neoplastic) are bcl-2 protein positive. Follicle centre cell lymphomas are also CD5 and CD43 negative. Both mantle cell lymphoma and B-CLL are positive for CD5 and CD43 and negative for CD10. They may both be positive for IgD. Mantle cell lymphomas are, however, invariably positive for cyclinD1 while the neoplastic cells of B-CLL, in common with those of SMZL, do not express this protein.30

HAIRY CELL LEUKAEMIA AND OTHER LYMPHOPROLIFERATIVE DISORDERS

Histology

It is important to distinguish hairy cell leukaemia (HCL) from other B cell lymphoproliferative disorders because treatment is completely different. The haematologist may rely almost entirely on the trephine, since hairy cells may be difficult to identify in the blood and the associated bone marrow fibrosis may yield a ‘dry tap’. HCL should be considered in the differential diagnosis of any unexplained cytopenia, particularly in the presence of splenomegaly.

HCL cells in the marrow may have a variety of appearances. The classic appearance in heavily involved marrows is of cells with oval to bean-shaped bland nuclei and abundant pale or clear cytoplasm giving a ‘fried egg’ appearance to the cells. This contrasts with other small cell lymphoproliferative disorders in which the cytoplasm is scanty and the nuclei tend to the circular (with or without irregularity). Another classic appearance is as spindled fibroblast-like cells.

Again, this appearance is rarely seen with other lymphomas. Finally, in very early involvement, the hairy cells may be present as innocuous interstitial oval or spindle shaped cells mixed with haemopoietic elements. HCL takes on a diffuse or interstitial pattern, in contrast the nodular pattern characteristic of other lymphomas is almost never seen in HCL.

In the spleen, HCL is even more characteristic, showing predominantly red pulp infiltration in contrast to the white pulp involvement in all other B cell lymphoproliferative disorders (including splenic marginal zone lymphoma, which may resemble HCL morphologically in the peripheral blood smear). The cytological features described above are similar in the spleen. Of note, hairy projections seen in cytological smear preparations are not evident in tissue sections.

Immunophenotype

HCL is always positive for B cell markers such as CD20 and CD79a, and is always CD5 and CD10 negative. The marker DBA44 is a very sensitive marker for HCL, but it may be positive in other B cell lymphoproliferative disorders and thus should not in isolation be used as a specific marker for HCL (Fig. 6).31 DBA44 is more useful in demonstrating subtle minimal disease in treated HCL patients. Tartrate resistant acid phosphatase (TRAP), previously only available on fresh cells, is now available as an immunostain for paraffin sections, and is quite specific for HCL.32 Finally, HCL cells coexpress CD68, which would be unusual in other B lymphoproliferative disorders. Nevertheless, unless morphology is characteristic, correlation with flow cytometric analysis of peripheral blood cells (these can be concentrated in a buffy coat if necessary) or bone marrow aspirate cells is...
strongly recommended for definite diagnosis in HCL. Using flow cytometry, HCL cells have a classic phenotype of expression of CD25, CD11c and CD103.

REFERENCES