Diagnostic Algorithm of Common Mature B-Cell Lymphomas by Immunohistochemistry

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- **Context.**—Different types of mature B-cell lymphomas, including plasma cell neoplasms, exhibit distinct immunohistochemical profiles, which enable them to be correctly diagnosed. However, except for rare examples of lymphoma-specific immunohistochemistry, such as cyclin D1 in mantle cell lymphoma and annexin A1 in hairy cell leukemia, immunohistochemical profiles of mature B-cell lymphomas overlap and lack specificity.

- **Objectives.**—To systematically review immunohistochemical features associated with commonly encountered mature B-cell lymphomas based on the presence or absence of CD5 and CD10; to review the immunophenotypic profile of plasma cells derived from plasma cell myelomas and B-cell lymphomas; and to review a group of rare, aggressive B-cell lymphomas with antigen expression features of plasma cells.

- **Data Sources.**—Published and PubMed-indexed English literature was reviewed.

Immunophenotyping with immunohistochemistry (IHC) remains an essential diagnostic tool for mature lymphomas, in combination with cytogenetics, molecular genomics, and clinical, radiologic, and other laboratory tests. As a technique, IHC is relatively easy to perform and is readily available in diagnostic laboratories compared with flow cytometry (FC), genetics, and molecular studies. Although FC is fast and requires less material, IHC is advantageous because the immunohistochemical profiles and cytomorphic features can be evaluated simultaneously.

Non-Hodgkin lymphomas can be classified into B-cell, T-cell, and natural killer–cell lymphomas according to lineage assignment, immaturity/maturity, genetics, immunophenotype, cell size, growth pattern, and clinical features. In this review, we focus on the utility of IHC in diagnosing mature B-cell lymphomas only.

**CD5+/CD10− B-CELL LYMPHOMA**

The classic prototypes of CD5+/CD10− B-cell lymphomas are small lymphocytic lymphoma (SLL) and mantle cell lymphoma (MCL). Small lymphocytic lymphoma and chronic lymphocytic leukemia (CLL) are 2 different presentations of the same disease. According to the International Workshop on Chronic Lymphocytic Leukemia, the diagnostic criteria for SLL are lymphadenopathy, absence of cytopenia because of bone marrow infiltration by CLL/SLL, and fewer than 5 × 10⁹/L peripheral blood B cells.¹

Although CLL is the most common leukemia affecting adults in Western countries,² according to a recent study, CLL/SLL is the second most frequent B-cell malignancy, accounting for 18.6% of non-Hodgkin lymphomas in the United States.³ According to published data, 80% to 92% of CLLs stain positive for CD5,⁴ but the exact percentage of SLL that is positive for CD5 is not known. Apart from CD5, SLL is typically positive for other B-cell antigens, such as CD19, CD20, CD22, CD23, CD79a, PAX5, and surface light-chain immunoglobulins. In addition, SLL is negative for CD10, CD81, and FMC-7, and negative to dimly positive for CD79b. Notably, compared with other non-CLL/SLLs, SLL/CLL is often dimly positive for B antigens, which are helpful in distinguishing CLL/SLLs from other CD5+ non-CLL/SLLs. In addition, the CD23/FMC-7− sets CLL/SLL apart from MCL in most, but not all, cases.
Similar to SLL/CLL, most (93%–95%) of MCLs are positive for the antigen CD5.6,7 Besides CD5, MCL expresses all other B-cell antigens, including CD19, CD20, CD22, CD79a, CD79b, FMC-7, and PAX5. Mantle cell lymphoma is usually, but not always, negative for BCL6, CD10 (see below), and CD23. Almost all MCLs, including rare CD5− ones, are positive for cyclin D1, also known as BCL1, CCND1, or PRAD1.5,8 Cyclin D1 is a member of the cyclin D protein family.5,9 B cells from the mantle zone are negative for cyclin D1. Thus, MCL in situ is usually an incidental finding, and cyclin D1 IHC is required to recognize such rare cases (Figure 1, A).11,12

Cyclin D1+ MCL is easily diagnosed, regardless of CD5 immunoreactivity. However, diagnosis of cyclin D1− MCL is challenging. Several studies have shown that SOX11,13,14 cyclin D2, and/or cyclin D315,16 are positive in these cases. Importantly, neither cyclin D2 nor cyclin D3 is specific for MCL,17 but nuclear expression of SOX11 is a specific marker associated with MCL, according to Chen et al18 (Figure 1, B and C).

Lymphoplasmacytic lymphoma (LPL) is a rare type of non-Hodgkin lymphoma usually involving bone marrow, and less frequently, the lymph nodes and spleen. Although, in LPL, CD5 expression is anecdotal by IHC,19 positive expression of CD5 on the monotypic B cells ranges from 9% to 43% based on FC studies.20,21

Marginal zone B-cell lymphoma (MZBCL) has 3 morphologic types based on the sites involved, namely, nodal, splenic, and extranodal MZBCL of mucosa-associated lymphoid tissue (MALT lymphoma). In contrast to the higher rates of nodal MZBCLs expressing CD5 (8.6%),22 less than 1% of MALT lymphomas are positive for CD5.23 Splenic MZBCLs exhibit positive CD5 expression in about 20% of the cases.24,25 CD5+ splenic MZBCL is closely related to its classic CD5− counterpart, except for higher lymphocyte counts at diagnosis and more-diffuse bone marrow infiltration.26

From the 2 types of diffuse large B-cell lymphomas (DLBCLs) expressing CD5, namely, de novo and transformed/secondary DLBCLs, only CD5+ de novo DLBCL, not otherwise specified (NOS), is reviewed in detail here. Approximately 10% of DLBCLs NOS are CD5+ de novo DLBCLs (Figure 2, A through D).27 These lymphomas have higher rates of BCL2 expression (Figure 2, E) and recurrence in the central nervous system and are more likely to exhibit a nongerminall center B-cell phenotype28,29 (Figure 2, F through H). Although there is no cytomorphologic difference between CD5+ and CD5− DLBCL NOS, cyclin D2 has been reported to be highly specific for de novo CD5+ DLBCL.30 For practical diagnostics, the pleomorphic variant of MCL and the DLBCL variant of the Richter transformation from CLL/SLL should be ruled out in CD5+ B-cell lymphomas with medium to large cell sizes. The CD5+/CD10− B-cell lymphomas are summarized in Table 1.

**Figure 1.** Mantle cell lymphoma (MCL) in situ and SOX11 expression. A, A case of MCL in situ in which cyclin D1+ cells are limited in the mantle zone without thickening. B and C, A Case of MCL with nuclear staining of SOX11 (panels B and C are courtesy of Yi-Hua Chen, MD, Department of Pathology, Northwestern University, Chicago, Illinois (original magnifications ×40 [A] and ×200 [B and C]).

**CD10+/CD5− B-CELL LYMPHOMA**

Follicular lymphoma (FL) and Burkitt lymphoma (BL) are the 2 prototypical B-cell lymphomas expressing CD10. In FL, the extent of CD10 expression varies by grade, even within the same tumor. For example, CD10 is expressed in 80% of grade 1 versus 17% of grade 3 FLs.31 In addition, CD10 expression is greater in neoplastic cells from intrafollicular than from interfollicular regions.32 CD10 is typically negative in FLs with marginal zone differentiation (Figure 3, A through F).32 In addition to CD10, BCL2, an antiapoptotic protein, is useful in differentiating FL from reactive follicular hyperplasia, but expression of BCL2 depends on grade and location. For instance, although 85% to 90% of low-grade (grades 1 and 2) FLs express BCL2, only 50% of grade 3 FLs are positive for BCL2.33 However, FLs testing negative for BCL2, based on standard...
Figure 2. CD5+ de novo diffuse large B-cell lymphoma, not otherwise specified with nongerminall center phenotype. A, Centroblast-like, atypical lymphoid cells with frequent mitosis and scattered apoptotic bodies. B through E, Atypical lymphoid cells are positive for CD20 (B) and negative for CD3 (C) but have an aberrant expression of CD5 (D) and BCL2 (E). F through H, The atypical cells are positive for BCL6 (F) and MUM1 (G) but negative for CD10 (H) and BCL1 (data not shown) (hematoxylin-eosin, original magnification ×200 [A]; original magnification ×200 [B through H]).
Table 1. Expression Pattern and Frequency of CD5 and CD10 in Common, Mature B-Cell Lymphomas

| Immunophenotype | Type of Mature B-Cell Lymphoma | Approximate % Staining | Source, y |
|-----------------|--------------------------------|-------------------------|----------|
| CD5+/CD10-      | MCL                            | 93-95                   | Dorfman and Shabsigh,9 1977; Gualco et al,7 2010 |
|                 | SLL/CLL                        | 80-92                   | Kurec et al,4 1992; Geiler et al,3 1991 |
|                 | LPL                            | 9-43                    | Hunter et al,20 2005; Morice et al,21 2009 |
|                 | Splenic MZBCL                  | 20                      | Gimen et al,24 2005; Matutes et al,25 2008 |
|                 | Nodal MZBCL                    | 8.6                     | Jaso et al,23 2013 |
|                 | MALT lymphoma                  | 1                       | Jaso et al,23 2012 |
|                 | De novo DLBCL NOS              | 10                      | Tagawa et al,7 2005 |
|                 | BL                             | 100                     | Dogan et al,7 2000 |
|                 | FL (low grade)                 | 80                      | Eshoa et al,31 2001 |
|                 | DBLCL, NOS                     | 10-40                   | Colomo et al,66 2003; Berglund et al,47 2005; Visco et al,48 2012 |
|                 | HCL                            | 10-20                   | Jasonowski et al,43 2003; Gupta et al,44 2015 |
|                 | FL (grade 3)                   | 17                      | Eshoa et al,31 2001 |
|                 | MCL                            | 0-7                     | Akhter et al,45 2015 |
| CD10+/CD5-      | MALT lymphoma                  | >99                     | Jaso et al,23 2012 |
|                 | Nodal MZBCL                    | 92                      | Jasos et al,23 2013 |
|                 | Splenic MZBCL                  | 80                      | Gimen et al,24 2005; Matutes et al,25 2008 |
|                 | LPL                            | 57-91                   | Hunter et al,20 2005; Morice et al,21 2009 |
|                 | HCL                            | 80-90                   | Jaso et al,43 2003; Gupta et al,44 2015 |
|                 | DBLCL, NOS                     | 50-70                   | Colomo et al,66 2003; Berglund et al,47 2005; Visco et al,48 2012 |
|                 | FL (grade 3)                   | 83                      | Eshoa et al,31 2001 |
|                 | FL (low grade)                 | 20                      | Eshoa et al,31 2001 |
|                 | SLL/CLL                        | 8-20                    | Kurec et al,4 1992; Geiler et al,3 1991 |

Abbreviations: BL, Burkitt lymphoma; CLL, chronic lymphocytic leukemia; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; HCL, hairy cell leukemia; LPL, lymphoplasmacytic lymphoma; MALT, mucosa-associated lymphoid tissue; MCL, mantle cell lymphoma; MZBCL, marginal zone B-cell lymphoma; NOS, not otherwise specified; SLL, small lymphocytic lymphoma.

antibodies for residues 41 to 54, can test positive for BCL2 when different antibodies are used.34 Primary cutaneous follicle center lymphoma is typically negative for BCL2.35

In our opinion, a minimal IHC panel for FL should include BCL2, CD3, CD10, and CD20; however, ideally, BCL6, CD5, and CD21 should be included as well. Recently, new germinal center (GC)-associated markers, such as GCET1, HGAL, and LMO2, have been introduced. Among these 3 markers, GCET1 shows the highest specificity for FL (60% of cases). Both HGAL and LMO2 lack specificity for FL, although they show stronger staining in FL compared with other types of mature B-cell lymphomas.36

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Hairy cell leukemia (HCL) and MCL can occasionally be confused with each other; however, the combination of CD10 and CD5 expression is unique to MCL. MCL is characterized by CD10 positivity in approximately 10% to 20% of HCL cases.43,44 A similar percentage has been reported by Gualco et al7 when different antibodies are used.34 Primary cutaneous follicle center lymphoma is typically negative for BCL2.35
useful in diagnosing B-cell malignancies including MALT lymphoma. This addition is particularly important for cases with scant amounts of diagnostic materials, such as those from core needle biopsies or those associated with plasmacytic differentiation. Positive CD43 expression can be detected in 20% to 40% of MALT lymphomas. Aberrant coexpression of CD43 by neoplastic B cells in MALT lymphoma can be site/location dependent. For example,
Arends et al. found that CD43 was not helpful in discriminating gastric MALT lymphoma from chronic gastritis. Normal B cells from the terminal ileum, especially Peyer patches, are positive for CD43. CD21 and another dendritic cell antigen, CD35, but not CD23, can aid in the diagnosis of MALT lymphoma in 2 ways. First, MALT lymphoma cells usually express CD21. Second, the characteristics of follicular dendritic meshwork, including size, contour, uniformity, and density, serve as additional indicators of MALT lymphoma. Sometimes MZBCL and SLL/CLL can exhibit plasmacytic differentiation. Plasmacytic differentiation is detected in approximately 33% of MALT lymphomas (Figure 6, A through F). This feature not only assists in making the correct diagnosis but also helps in monitoring the disease status after treatment.

In contrast to MZBCL, LPL always contains a component of monotypic plasma cells (PCs), as the name indicates. Although MZBCL and LPL share many overlapping immunophenotypic features, the immunoglobulin heavy chain expressed by monotypic PCs from LPL is nearly always immunoglobulin (Ig) M, in contrast to the typical IgM expressed in MZBCL. Lymphoplasmacytic lymphoma is diagnosed by exclusion, and at times, MZBCL and LPL cannot be distinguished based on morphologic and immunophenotypic features; in those cases, a positive MYD88 L265P somatic mutation found in most LPLs can be employed. Notably, as demonstrated by FC, the monotypic PCs derived from B-cell lymphoma have a similar immunophenotype to B cells and differ from those of PC myeloma.

Hairy cell leukemia is positive for all common B-cell antigens (CD19, CD20, CD79a, FMC-7, and PAX5), with characteristic expression of annexin A1 (Figure 7, A), CD11c,
CD25, CD103, CD123, DBA-44 (CD72) (Figure 7, B), the Hector Battifora mesothelial epitope-1 (HBME-1), pERK, T-bet, and TRAP58–61 but is typically negative for CD5 and CD10, although 10% to 20% of HCLs are positive for CD10.43,45 With the exception of annexin A1, which is a specific marker for HCL,58 the previously so-called HCL markers, including CD11c, CD103, DBA-44, and HBME-1, are not specific for HCL. They can be found in splenic, extranodal marginal zone B-cell lymphoma (MZBCL) with concomitant, monotypic plasmacytic differentiation. A, This extranodal MZBCL has a focal area of monocytoid differentiation (upper left) and plasmacytic differentiation (lower right corner). B through D, The plasma cells are positive for CD138 (B) and dimly positive for CD19 (C) but negative for CD20 (D). E and F, These plasma cells are positive for κ (E) but negative for λ (F) light chains (hematoxylin-eosin, original magnification ×100 [A]; original magnification ×200 [B through F]).

Figure 6. Extranodal marginal zone B-cell lymphoma (MZBCL) with concomitant, monotypic plasmacytic differentiation. A, This extranodal MZBCL has a focal area of monocytoid differentiation (upper left) and plasmacytic differentiation (lower right corner). B through D, The plasma cells are positive for CD138 (B) and dimly positive for CD19 (C) but negative for CD20 (D). E and F, These plasma cells are positive for κ (E) but negative for λ (F) light chains (hematoxylin-eosin, original magnification ×100 [A]; original magnification ×200 [B through F]).
diffuse red pulp small B-cell lymphoma and the HCL
together.60–62 Although annexin A1 is specific for HCL,58 its
expression in normal hematopoietic cells, especially in
neutrophils, makes it unsuitable for detection of minimal,
residual HCL, but T-bet was reported to be useful in those
cases.63 Weak cyclin D1 staining can be observed in most
HCLs (Figure 7, C), but there is no rearrangement of the
cyclin D1 gene at 11q13 locus.64

Figure 7. Expression of annexin A1, DBA-44, and BCL1 by hairy cell
leukemia (HCL). This HCL is the same case shown in Figure 4. A through C,
The atypical lymphoid cells are positive for annexin A1 (partial) (A), DBA-
44 (B), and BCL1 (partial) (C) (original magnification ×400 [A]; original
magnification ×200 [B]; original magnification ×200 [C]).

After excluding CD5+ and/or CD10+ DLBCL NOS, approximately 50% to 70% of de novo DLBCLs NOS are
negative for both CD5 and CD10. Similar to other mature B-
cell lymphomas, DLBCL NOS is positive for B-cell–specific
and the associated antigens with varying frequencies.65 As
mentioned, apart from CD10, 2 additional antigens, BCL6 and
MUM1, are included in the designation of GC versus
non-GC phenotypes of DLBCL in the Hans66 algorithm
with approximately 80% concordance with gene expression
profiling. By adding GCET1 and FOXP1, Choi et al67
increased the concordance of immunohistochemical classi-
fication of GC versus non-GC to 93%, as compared with
gene expression profiling.

Other rare CD5− and CD10− mature B-cell lymphomas are
CD5− MCLs and CD10− FLs. The CD5− MCLs are very rare
and account for only approximately 5% to 7% of MCLs.6,7
Cytologically, CD5− MCLs tend to display a marginal zone
or the so-called monocytoid differentiation.67,68 CD10− FL
was discussed previously. The CD5+/CD10− mature B-cell
lymphomas are summarized in Table 1.

**PC NEOPLASMS**

Plasma cell neoplasms encompass plasmacytoma, plasma
cell myeloma (PCM), monoclonal gammopathy of
undetermined significance, and monoclonal immunoglob-
ulin deposition diseases; the first 2 are reviewed here.
Apart from CD38 and CD138, neoplastic PCs derived from
PCM exhibit a different immunophenotype from PCs
derived from B-cell lymphomas, according to Seegmiller
et al.57 Among all the antigens studied with FC, CD19
provided the best criterion for distinguishing between
these 2 types of neoplastic PCs. In particular, neoplastic
PCs from B-cell lymphomas are positive for CD19 and are
almost always negative in neoplastic PCs from PCM.69 In
fact, less than 1% of PCM cases were positive for CD19.69
According to the authors,57,69 expression of CD20, CD45,
and CD56 was detected in 9.3% to 27%, 8.8% to 41%, and
71.7% of neoplastic PCs from PCM, respectively, as
compared with 32%, 91%, and 33%, respectively, in PCs
from B-cell lymphomas.57 The frequency of CD117
expression in PCs from PCMs detected with FC correlated
perfectly with IHC according to Pruneri et al,70 who
reported 28.2% immunoreactivity of CD117 among PCMs.
CD117 is very rarely expressed in B-cell lymphomas.71

Cyclin D1, a hallmark for MCL, is expressed in 30% to 35%
of PCMs and in 0% to 17% of plasmacytomas.9,72,73 As
summarized in Table 2, the combination of BCL1, CD19,
CD45, CD56, and CD117 is sufficient to distinguish PCs
derived from PCMs and/or plasmacytomas from B-cell
lymphomas, even in cases in which there is exuberant
plasmacytic differentiation.74

A recent report suggested that IgA-expressing nodal and
extranodal plasmacytoma may represent a distinct form of
extramedullary plasmacytoma characterized by young age,
frequent nodal involvement, and low risk of progression to
PCM.75 Plasmablastic PCM shares similar immunohisto-
chemical profiles with PCM, which are described below.

**AGGRESSIVE B-CELL LYMPHOMA WITH
IMMUNOPHENOTYPIC OR MORPHOLOGIC FEATURES
OF PLASMABLASTS**

B-cell lymphomas in this category include plasmablastic
PCM; plasmablastic lymphoma (PBL); primary effusion
lymphoma (PEL), including the extracavitary variant; large
B-cell lymphoma arising in HHV8-associated multicentric Castleman disease, and ALK⁺ large B-cell lymphoma. The antigens CD38, CD138, and MUM1 are positive in all cases of plasmablastic PCM, PBL, and PEL. However, plasmablastic PCM and PBL cannot be separated from each other based on an IHC panel that includes CD45, CD79a, CD56, and PAX5, according to Vega et al; however, EBV was found to be 100% positive in 9 cases of PBL but negative in 7 cases of plasmablastic PCM. In our opinion, CD19 should be included in this panel, which may aid in distinguishing these 2 lymphomas.

An extensive, large-scale immunohistochemical characterization of PEL has not, to our knowledge, been reported in the literature because PEL typically presents as body cavity effusions, rather than tissue masses, except for extracavitary PEL. The FC studies we conducted showed that CD38, CD71, and CD30 were positive in 100% of PELs. Although PEL, including its solitary variant and large B-cell lymphoma arising in HHV8-associated multicentric Castleman disease, are both positive for HHV8, the latter is typically negative for CD138 and EBV, which distinguishes this type of aggressive B-cell lymphoma from traditional PBL. ALK⁺ large B-cell lymphoma is a rare, aggressive B-cell lymphoma, which can be difficult to diagnose, and is typically negative for most of the common B-cell antigens but positive for PC markers such as CD138, VS38, EMA, and MUM1. The immunophenotypic features of plasmablastic PCM, PBL, PEL, and ALK⁺ large B-cell lymphoma are summarized in Table 3.

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### Table 2. Immunohistochemical Characteristics of “Plasma Cells” From B-Cell Lymphomas and Plasma Cell Myelomas (PCMs)

| BCL1 | CD19 |
|------|------|
| Source, y | Source, y |
| P/N staining (% staining) | P/N staining (% staining) |
| B-cell lymphomas | N (except in MCL and HCL) | P (~95) |
| PCMs | P (30–35) | Molina et al, 2011 |
| | Pruneri et al, 2006; Bravo et al, 2000 | (~<1) |
| | | Seegmiller et al, 2007 |

Abbreviations: -, approximately; HCL, hairy cell leukemia; MCL, mantle cell lymphoma; N, negative; P, positive.

### Table 3. Immunophenotypic (Immunohistochemistry [IHC] and Flow Cytometry [FC]) Comparison Between Plasmablastic Plasma Cell Myeloma (PCM), Plasmablastic Lymphoma (PBL), Primary Effusion Lymphoma (PEL), and Anaplastic Lymphoma Kinase 1 (ALK⁺) Large B-Cell Lymphoma (LBCL)

| Plasmablastic PCM (IHC), n/N (%) | PBL (IHC), n/N (%) | PEL (FC), n/N (%) | ALK⁺ LBCL (IHC), n/N (%) |
|----------------------------------|---------------------|------------------|--------------------------|
| CD38 | 7/7 (100) | 9/9 (100) | 12/12 (100) | ND |
| CD138 | 7/7 (100) | 19/19 (100) | ND | 56/57 (98) |
| MUM1 | 7/7 (100) | 8/8 (100) | ND | 14/14 (100) |
| cK or cL restriction | 6/7 (86) | 7/21 (33) | 3/6 (50) | 43/72 (60) |
| BCL2 | 4/7 (57) | 3/8 (38) | ND | ND |
| CD56 | 3/7 (43) | 5/9 (56) | ND | ND |
| CD45 | 2/6 (33) | 16/21 (76) | 12/12 (100) | 38/45 (84) |
| CD10 | 2/7 (29) | 6/9 (67) | ND | ND |
| CD4 | 1/5 (20) | 2/5 (40) | 2/12 (17) | 22/34 (65) |
| CD117 | 1/7 (14) | 0/4 (0) | ND | ND |
| ALK1 | ND | ND | ND | 30/30 (100) |
| Bob1 | ND | ND | ND | 16/16 (100) |
| BCL6 | 0/7 (0) | 1/16 (6.3) | ND | ND |
| CD19 | ND | ND | 0/12 (0) | ND |
| CD20 | 0/7 (0) | 0/21 (0) | 2/12 (17) | 1/56 (1.8) |
| CD30 | 0/5 (0) | 0/7 (0) | 10/12 (83) | 3/55 (5.5) |
| CD45RO | ND | ND | 7/8 (88) | ND |
| CD71 | ND | ND | 12/12 (100) | ND |
| CD79a | 0/2 (0) | 1/6 (17) | ND | 12/54 (22) |
| EMA | ND | ND | ND | 47/53 (89) |
| HLA-DR | ND | ND | 6/8 (75) | ND |
| OCT2 | ND | ND | ND | 13/16 (81) |
| PAX5 | 0/6 (0) | 2/18 (11) | ND | 5/18 (2.8) |
| EBV (ISH) | 0/7 (0) | 17/17 (100) | 5/9 (56) | 0/18 (0) |
| HHV8 | 0/6 (0) | 1/5 (20) | 10/10 (100) | ND |
| Ki-67 | (79) (87) | ND | ND | NK |

Abbreviations: cK, cytoplasmic kappa; cL, cytoplasmic lambda; EBV, Epstein-Barr virus; EMA, epithelial membrane antigen; HHV8, human herpesvirus 8; ISH, in situ hybridization; ND, not done; NK, not known.

a Source: Vega et al, 2005.
b Source: Vega et al, 2005; and Dong et al, 2005.
c Source: Wang et al, 2010.
d Source: Reichard et al, 2007; and Pan et al, 2016.
e Cited article (Vega et al, 2005) was published in 2005 when HHV8 positivity was acceptable in PBL.
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Table 2. Extended

| CD5 | CD56 | CD117 |
|-----|-----|-----|
| P (≈91) | Molina et al,2011 | Molina et al,2011 | Very rarely |
| P (8.8–41) | Molina et al,2011; Seegmiller et al,2007 | Treon et al,2012; Seegmiller et al,2007 | Lin et al,2004 |
| Source, y | Source, y | Source, y |
| P (~33) | P (~7.1) | P (~28) | Mansoor et al,2007 |

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