B-cell Non-Hodgkin Lymphomas with Plasmacytic Differentiation

Charles M. Harmon, MD[a], Lauren B. Smith, MD[b,*]

KEYWORDS

• Lymphoplasmacytic • MALT • Nodal marginal zone • Splenic • Plasmablastic • Plasmacytic • Lymphoma

Key points

- Significant overlap exists between low-grade B-cell lymphomas with plasmacytic differentiation.
- Testing for *MYD88* (L265P) can be a useful adjunct in differentiating lymphoplasmacytic lymphoma (LPL) from other small B-cell lymphomas with plasmacytic differentiation when morphologic and immunophenotypic findings are equivocal.
- Cases of immunoblastic morphology raise a broad differential diagnosis, including immunoblastic diffuse large B-cell lymphoma (I-DLBCL), plasmablastic lymphoma, ALK-positive large B-cell lymphoma (ALK^+ LBCL), and the solid variant of primary effusion lymphoma (PEL).
- Clinicopathologic correlation may be necessary to distinguish plasmablastic lymphoma (PBL) from anaplastic plasmacytoma because the morphologic features and immunophenotype can be similar.

ABSTRACT

B-cell non-Hodgkin lymphomas with plasmacytic differentiation are a diverse group of entities with extremely variable morphologic features. Diagnostic challenges can arise in differentiating lymphoplasmacytic lymphoma from marginal zone lymphoma and other low-grade B-cell lymphomas. In addition, plasmablastic lymphomas can be difficult to distinguish from diffuse large B-cell lymphoma or other high-grade lymphomas. Judicious use of immunohistochemical studies and molecular testing can assist in appropriate classification.

LYMPHOPLASMACYTIC LYMPHOMA

OVERVIEW

LPL is a B-cell lymphoma composed of a spectrum of small B lymphocytes, plasmacytoid lymphocytes, and plasma cells.[1] According to the 2008 World Health Organization (WHO) classification scheme, LPL is a diagnosis of exclusion because its definition is that of a lymphoma "which does not fulfill the criteria for any of the other small B-cell lymphoid neoplasms."[1] Mutations in the *MYD88* gene, however, that result in an amino acid change (L265P), have recently been identified in approximately 90% of cases of LPL.[2–8] Although most patients with LPL have an immunoglobulin M (IgM) paraprotein, some patients may have a non-IgM paraprotein, whereas others may not have any detectable paraprotein. Although the terms, *LPL* and *Waldenström macroglobulinemia (WM)* are sometimes used interchangeably, WM is a clinicopathologic entity that is defined as LPL with an IgM paraprotein and bone marrow (BM) involvement.[1] Thus, although all cases of WM are also LPL, a minority of cases of LPL do not satisfy criteria for a diagnosis of WM.

LPL is a disease of older adults, with a median age at diagnosis of 63 years in African Americans

The authors have no relevant personal financial relationships or financial conflicts of interest to disclose.
[a] Department of Pathology, University of Michigan Hospitals and Health Systems, 1301 Catherine Street, Ann Arbor, MI 48109, USA; [b] Department of Pathology, University of Michigan Hospitals and Health Systems, 5320 Medical Science I, 1301 Catherine Street, Ann Arbor, MI 48109-5602, USA
* Corresponding author.
E-mail address: lbsmith@med.umich.edu

Surgical Pathology 9 (2016) 11–28
http://dx.doi.org/10.1016/j.path.2015.09.007
1875-9181/16/$ – see front matter

and of 73 years in white patients.[9] There is a male predominance, and the disease is more common in whites than in blacks.[10] Although the most common presenting symptom is fatigue related to anemia, the presence of an IgM paraprotein may also result in peripheral neuropathy, hemolytic anemia, coagulopathy, cryoglobulinemia, and hyperviscosity.[10]

GROSS AND MICROSCOPIC FEATURES

LPL most commonly involves the BM with less frequent involvement of lymph nodes and spleen.[1] Rarely, LPL presents as a primarily node-based lymphoma. BM involvement by LPL manifests histologically as an interstitial infiltrate sometimes mixed with nodular and paratrabecular aggregates.[11] Less commonly, LPL involves the BM in a diffuse pattern. The infiltrate of LPL morphologically consists of a mixture of small lymphocytes, plasmacytoid lymphocytes, and plasma cells (**Fig. 1**). Although nonspecific, the presence of intermixed mast cells and hemosiderin is characteristic of LPL.[12]

Lymph node involvement by LPL is most commonly characterized by a lymphoplasmacytic infiltrate within the paracortex and in the parasinusoidal regions with patent sinuses and relative sparing of the lymph node architecture. Proliferation centers, which are a characteristic feature of nodal involvement by chronic lymphocytic leukemia/small lymphocytic leukemia (CLL/SLL), are not seen in LPL.[1] Prominent monocytoid features and follicular colonization are also typically absent in LPL and are more commonly seen in marginal zone lymphoma (MZL).[12] As in the BM, intermixed mast cells and hemosiderin are often present (**Box 1**).

In contrast to other small B-cell lymphomas, the immunophenotypic profile of LPL is not distinctive and displays significant overlap with other B-cell lymphoproliferative disorders.

The small B-lymphocytes of LPL express pan-B-cell markers, including CD19, CD20, CD22, CD79a, and PAX5. LPL is usually negative for CD10, CD5, and CD23. Dim or partial expression of CD5 and/or CD23 may be seen, however, in LPL, with occasional coexpression of these markers.[13,14] The plasma cells of LPL almost always express CD45, CD19, CD38, and CD138. Although the plasma cell component usually demonstrates cytoplasmic immunoglobulin light chain restriction, polytypic expression of light chains is seen in a small minority of cases.[13] In contrast to non-neoplastic plasma cells, plasma cell myeloma (PCM), and MZL with plasmacytic differentiation, a portion of the plasma cells in LPL may aberrantly coexpress PAX5 with CD138.[13,15]

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

As discussed previously, the diagnosis of LPL requires exclusion of other small B-cell lymphomas with plasmacytic differentiation, including MZL, follicular lymphoma (FL), and CLL/SLL. Less commonly, mantle cell lymphoma (MCL) may

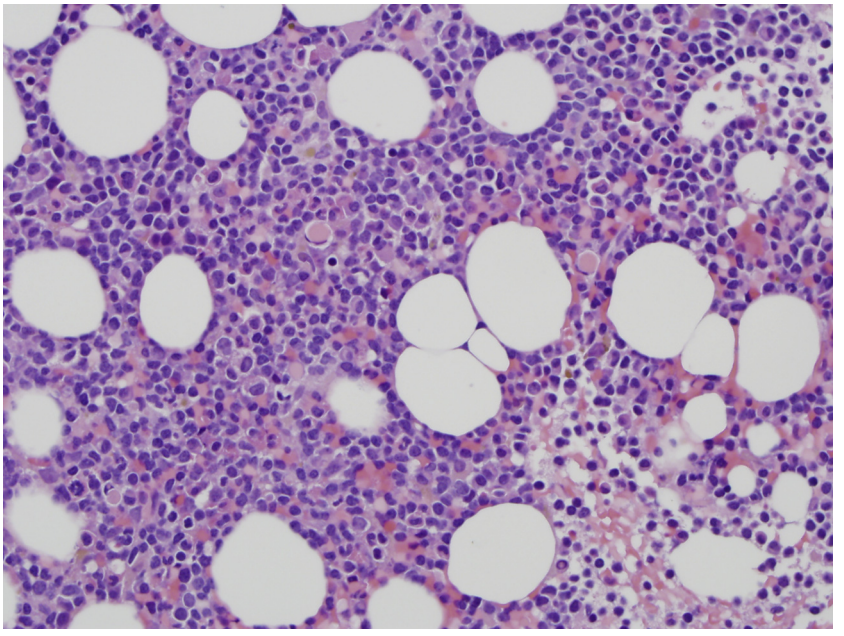

Fig. 1. BM biopsy showing an infiltrate of small lymphocytes and plasma cells, including occasional Dutcher bodies, in a case of LPL (hematoxylin-eosin, original magnification ×400).