Lymphoplasmacytic lymphoma – Pathological Features

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Definition

Lymphoplasmacytic lymphoma (LPL) is a neoplasm of small B lymphocytes, plasmacytoid lymphocytes, and plasma cells, usually involving bone marrow and sometimes lymph nodes and spleen, which does not fulfill criteria for other small B-cell neoplasms with plasmacytic differentiation. Waldenström macroglobulinemia (WM) is LPL with bone marrow involvement and an IgM monoclonal gammopathy of any concentration.

Etiology

About20% of cases are familial. Hepatitis C virus (HCV) is associated in some series. Chronic immunologic stimulation (Sjogren's syndrome, scleroderma, autoimmune hemolytic anemia) may be associated with an increased risk of LPL/WM. Mast cells may help drive the proliferation.

Morphology

Bone marrow contains aggregates and/or a diffuse infiltrate of small lymphocytes, plasma cells and plasmacytoid lymphocytes, Dutcher bodies and increased mast cells. Lymph nodes usually show retention of architecture with a subtle B-cell infiltrate and few transformed cells; there may be epithelioid histiocyte clusters or in some cases, numerous immunoblasts. Proliferation centers and marginal zone differentiation are absent. There may be amyloid, immunoglobulin deposition, or crystal-storing histiocytes. Spleens demonstrate a red pulp lymphoplasmacytic infiltrate that may be nodular or diffuse.

Immunophenotype

Surface Ig and cytoplasmic Ig are expressed (IgM> IgG>> IgA). B cells are typically IgD-, express pan-B antigens (CD19, CD20, CD22, CD79a, Pax5), are often CD25+ CD38+ and are typically CD5-, CD10-, CD11c-, CD103-. CD23 is expressed in 30-60% of the cases. Up to 10% are CD5+ and about 5% CD10+. Plasma cells are CD19+ (unlike those in most myelomas), Mum1+, CD138+.

Genetics

IG genes are rearranged; *V* regions are hypermutated but lack ongoing mutations. There may be biased *VH* usage. Translocations involving *IGH* on chromosome 14 are not seen. Deletion 6q is reported in over half of bone marrow-based cases but is not specific. Trisomy 4 is reported in about 20%. Mutations in *MYD88* occur in over 95% of WM cases, and only rarely in other B-cell neoplasms with plasmacytic differentiation. WM has a homogeneous gene expression profile, independent of 6q deletion, which is more similar to that of normal B cells than to CLL or plasma cell myeloma; IL6 is consistently upregulated. WM cells have increased expression of miRNA-206 and reduced expression of miRNA-9*, leading to decreased histone acetylation.

Postulated normal counterpart

Memory B cell that differentiates to plasma cells

Pathological predictive factors
Cases with increased immunoblasts have an adverse prognosis; however, a validated grading system does not exist. Del6q may be associated with an adverse prognosis. Transformation to diffuse large B-cell lymphoma or Hodgkin lymphoma may occur, with poor survival.

Differential diagnosis
The differential diagnosis includes other small B-cell neoplasms with plasmacytic differentiation (CLL/SLL, MZL, MM). A combination of morphology (proliferation centers) and immunophenotype (CD5, CD23, CD20 and light chain intensity) usually suffice to distinguish LPL from CLL. Most MM are CD20- and class-switched; problems include CD20+ or IgM+ MM and class-switched LPL. A neoplastic B-cell component (CD20+ Pax5+ CD138-) and expression of CD19 by plasma cells favors LPL. MZL may be distinguished by morphology (marginal zone/monocytoid cells) and clinical features (extranodal, splenic) but occasionally the diagnosis may be "B-cell lymphoma with plasmacytic differentiation." Detection of *MYD88* mutations should be useful in this differential.

Variant: Gamma heavy chain disease
Gamma heavy chain disease is usually associated with a lymphoma that fulfills criteria for LPL involving lymph nodes, marrow, liver, spleen and peripheral blood. The clinical course is probably more aggressive than that of IgM-producing LPL.