Lymphoplasmacytic lymphoma – Pathological Features
Nancy Lee Harris, M.D.

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 defined as LPL with bone marrow involvement and an IgM monoclonal gammopathy of any concentration.

Etiology Up to 20% of cases may be familial. Hepatitis C virus (HCV) is associated with LPL in some series. Mast cells may help drive the proliferation.

Morphology Involved tissues contain small lymphocytes, variable numbers of plasma cells and plasmacytoid lymphocytes, Dutcher bodies and increased mast cells. In most cases, lymph nodes show retention of architecture with few transformed cells; there may be epithelioid histiocyte clusters or 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 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), are often CD25+ CD38+, and are CD5-, CD10-, CD103- and CD23-. Plasma cells are Mum1+ CD138+.

Genetics Ig genes are rearranged; V regions show somatic hypermutation but lack ongoing mutations. There may be biased VH usage. Deletion 6q is reported in over half of bone marrow-based cases but it is not specific. Trisomy 4 is reported in about 20%. WM is reported to have a homogeneous gene expression profile, independent of 6q deletion, which is more similar to CLL and normal B cells than to myeloma.

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.

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.