DESPITE APPARENT MORPHOLOGIC AND IMMUNOPHENOTYPIC HETEROGENEITY, WALDENSTRÖM MACROGLOBULINEMIA IS CONSISTENTLY COMPOSED OF CELLS ALONG A MORPHOLOGIC CONTINUUM OF SMALL LYMPHOCYTES, PLASMACYTOID LYMPHOCYTES, AND PLASMA CELLS.

Ellen D. Remstein[1], Paul J. Kurtin[1], Robert A. Kyle[2], Janice M. Hodnefield[1], Curtis A. Hanson[1].
[1]Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN, USA.
[2]Department of Internal Medicine, Mayo Clinic, Rochester, MN, USA.

We studied the clinical, morphologic, and immunophenotypic features of 26 cases of Waldenström macroglobulinemia (WM). WM was defined by an IgM-spike of ≥3.0 g/dL coupled with a clonal lymphocyte population in the bone marrow (BM) or peripheral blood (PB). There were 18 men and 8 women, with a median age of 64 years. Seventeen patients were anemic, 5 were neutropenic, and 8 were thrombocytopenic. Four patients had an absolute lymphocytosis and 5 had hyperviscosity (>4 cP). Neoplastic lymphoid cells were identified morphologically in 11/21 PB smears (52%), 18/19 BM aspirates (95%), and 24/25 BM biopsies (95%), and by flow cytometry (FC) in all cases tested, including 4 PB and 1 BM that were negative by morphology. The neoplastic cells were consistently composed of a spectrum of small lymphocytes, plasmacytoid lymphocytes, and plasma cells, although the dominant cell varied among these three cell types. BM biopsy involvement ranged from 20-90% and showed 4 histologic patterns: nodular (75%), interstitial (75%), paratrabecular (42%), and diffuse (4%). Several different patterns could be seen in the same biopsy specimen. Two histologic subtypes (lymphoplasmacytic (87%) and lymphoplasmacytoid (13%)) were identified. The polymorphous pattern was not seen. Several cytologic variants, including monocytoid (n=2), signet-ring cell (n=2), and hairy cell leukemia-like (n=1) were also identified. By FC, all cases showed immunoglobulin light chain restriction and expressed CD19 and CD20. Most cases (62%) lacked expression of CD5, CD10, and CD23. However, variants such as CD5+, CD23-, CD10- (n=3), CD5+, CD23+, CD10- (n=1) and CD5-, CD10+, CD23+/- (n=2), mimicking mantle cell lymphoma, chronic lymphocytic leukemia, and follicular lymphoma, respectively, were also seen. By paraffin section immunohistochemistry, the neoplastic cells in all cases expressed CD20 and/or CD79a, and they rarely exhibited weak focal expression of CD23, CD10, TRAP, and/or DBA.44. Cyclin D1 was uniformly negative. At last follow-up (median 36.5 months), 18/26 patients were alive. The median survival was 94 months. Causes of death included WM (n=1), large cell lymphoma transformation of WM (n=1), acute myeloid leukemia that was likely therapy related (n=2), and other/unknown causes.

In conclusion, when individual cases are compared, apparent morphologic diversity of WM is suggested. However, when it is recognized that every case of WM is comprised of cells along a morphologic continuum from small lymphocytes to plasma cells, a uniform and consistent pathology emerges. As WM shows immunophenotypic heterogeneity, it is important that morphology be the cornerstone of the diagnosis.