Intraclonal heterogeneity in LPL: A minority of concurrent monoclonal lymphocytes and plasmacytic cells sharing light chains are genetically related in putative lymphoplasmacytic lymphoma

Barbara K. Zehentner, Ph.D. HCLD (ABB)

Flow cytometric cell sorting combined with molecular gene rearrangement analysis can be used to further characterize simultaneously occurring phenotypically distinct B cell monoclonal lymphoid and monoclonal plasma cell populations.

In this study we analyzed bone marrow aspirate specimens of 38 LPL cases with identical light chain restriction for the monoclonal lymphoid and the plasma cell population. Monoclonality profiles were established for the lymphoid and the plasma cell populations by using flow cytometric cell sorting and subsequent monoclonal gene rearrangement analysis. Findings demonstrated that *related* genetic processes are less likely than *unrelated:* 13 of 38 specimens (34%) revealed identical genotypic profiles for the B lymphoid cells and the plasma cell population, while 25 (66%) featured non-identical profiles. The majority (12/13) of the genotypically identical group featured an immunophenotype consistent with Waldenström's/lymphoplasmacytic lymphoma (WM/LPL), while WM/LPL phenotype was present in 16/25 (64%) of the non-identical cases. In addition, we demonstrate the utility of flow cytometric cell sorting in combination with gene rearrangement and IgVH sequence analysis as well as plasma cell targeted FISH analysis in two clinical cases with presumed LPL/WM in which the presence of multiple distinct B cell and plasma cell populations was identified.

To establish the genetic relationship of concurrent clonal populations requires more detailed molecular analysis than surface Ig light chain status alone. The combination of flow cytometric cell sorting and molecular analysis can differentiate patients harboring one related clonal process versus two separate entities. Proof of an identical monoclonal genotype for plasmacytic and B-lymphoid cell populations could help define WM/LPL in the clinical setting of monoclonal lymphoid and plasma cells expressing the same light chains. Conversely, the confirmation of genotypically distinct populations can significantly improve confidence in diagnostic and prognostic decisions in specimens with B lymphoid lymphomas and a concurrent plasma cell neoplasm. These techniques add power to the diagnostic algorithm. The more specific diagnosis allows for greater accuracy in risk stratification/prognostic designation. Implementation of this method for routine clinical application in these diseases should be considered a valuable addition to current standard of care.