

Family Studies in Waldenstrom's macroglobulinemia (WM). McMaster ML, *National Institutes of Health, National Cancer Institute, Division of Cancer Epidemiology and Genetics, Genetic Epidemiology Branch; Bethesda, MD.*

Little is known about WM etiology or genetic and/or environmental determinants of susceptibility. Familial aggregation is difficult to substantiate, but familial clustering of WM has been documented for 40 years. We have undertaken a family study of WM to characterize its phenotypic spectrum, collect biologic and epidemiologic data, and establish a cohort suitable for linkage. We are studying families having A) ≥ 2 members with WM, or B) 1 case of WM if accompanied by ≥ 1 case of other LPD or clinical autoimmune disease. Study components include medical/family history questionnaires, full clinical evaluation, and bone marrow (BM) examination in selected patients for various studies, including molecular cytogenetics. Genetic studies will focus initially on candidate gene analyses; when sufficient informative families are accrued, linkage analysis will be conducted. To date, we have identified 50 eligible families, including 23 having ≥ 2 cases of WM, and have begun evaluating 21 cases and 50 first degree relatives from 10 families. Among cases, 63.2% are male, 36.8% female. Median age at diagnosis is 61.6 years. Nineteen (82.6%) produce an IgM κ paraprotein; 11 (47.8%) have suppression of IgG, IgA, or both. Among relatives, 7 (14%) exhibit a monoclonal gammopathy, usually IgM type; 30% have polyclonal gammopathy. Thirty-three (66%) have abnormal autoimmune markers; antithyroid (22.4%) antibodies are most common. BM cytogenetics demonstrate occasional abnormalities but no characteristic changes. Preliminary data suggest epidemiological and biological similarities between familial and sporadic WM. This study should help discern important clues to the etiology of WM and assist in refining the familial WM phenotype for linkage and other genetic studies, but continued accrual and evaluation of WM families is necessary to confirm these initial preliminary observations.