[Abstract 12]

LONG-TERM FOLLOW-UP OF FAMILIAL WALDENSTRÖM'S MACROGLOBULINEMIA KINDREDS

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Familial clustering of Waldenström's macroglobulinemia (WM) has been recognized for 40 years. Review of the literature shows that cross-sectional analyses of individual WM families have described laboratory abnormalities among WM cases and their relatives. The most striking finding has been the discovery of asymptomatic IgM monoclonal components (MC) in up to 6.3% of tested first-degree relatives of WM cases, representing a 10-fold increase relative to its estimated prevalence in the general population. Polyclonal increases and decreases in various immunoglobulin (Ig) levels have also been described. The significance of these findings is unknown, in part because there are no reliable prevalence estimates for polyclonal elevations and deficits in the general population and also in part because of evolving methodologies for Ig detection and quantification and plasticity in their interpretation. From these early studies, three first degree relatives found to have an IgM MC were reported individually in follow-up. In the case of an elderly woman, the IgM MC resolved within two years of its original documentation, whereas in the other two cases (who were siblings from a single family), WM was diagnosed 7 years and 15 years, respectively, after the discovery of an IgM MC. However, no systematic follow-up of any of these families has been done to document whether observed abnormalities have persisted or progressed over time. Three families with a total of 10 WM cases were referred to the Genetic Epidemiology Branch, National Cancer Institute, in 1977 (1 family) and 1987 (2 families). Consenting living cases and their first-degree relatives were evaluated with a series of electrophoretic and immunological studies. We will present results of prospective long-term (up to 27 years) follow-up of this family cohort. They provide a preliminary assessment of the prevalence and significance of observed Ig abnormalities in WM kindreds over time and a framework for the prospective long-term goals of the NCI WM family study.