

Evidence for the contribution of environmental exposures to the etiology of familial Waldenström macroglobulinemia

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Abstract

Linkage data and familial aggregation of Waldenström macroglobulinemia (WM) and related B-cell disorders suggest a role for genetic factors in WM etiology, but data addressing potential environmental influences have been limited. We designed a questionnaire-based study to examine the associations of clinical and environmental factors with WM in WM families with varying patterns of case aggregation. We analyzed data on 103 WM patients and 272 unaffected relatives from 35 multiple-case WM and 46 mixed WM/B-cell disorders kindred. We used logistic regression models to estimate odds ratios (ORs) and 95% confidence intervals (95% CIs) for association and accounted for familial clustering using a generalized estimating equations approach for the variance calculations. Models were additionally adjusted for age, gender, and family type (multiple-case WM or mixed WM/B-cell) as appropriate. In this study population, familial WM patients were more likely than unaffected relatives to report a history of autoimmune disease (OR 2.27; 95%CI=1.21-4.28) and infections (OR 2.13; 95%CI=1.25-3.64). Familial WM patients were also more likely to report exposure to farming (OR 2.70; 95%CI=1.34-5.42), pesticides (OR 2.83; 95%CI=1.56-5.11), wood dust (OR 2.86, 95%CI=1.54-5.33), and organic solvents (multiple case WM OR 4.21; 95%CI=1.69-10.51) compared to unaffected family members. While our study was exploratory, as it investigated a large number of exposures, these results provide clues to both genetic and environmental factors that may influence development of WM. We hypothesize that gene-environment interactions may contribute to WM etiology in at least a subset of familial WM. Future investigations should employ well-designed case-control studies to confirm these findings.