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First Name: Andres

Last Name: Ramirez-Gamero

Email: aframirasa@gmail.com

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Correlation Between Familial Waldenström Macroglobulinemia Clusters With Clinical Features, Complications, and Outcomes in 1000 Patients: A Single-Center Retrospective Cohort Study

Andres Ramirez-Gamero MD^{1,2}, Nicholas Tsakmaklis BA¹, Zachary R. Hunter PhD^{1,2}, Maria Luisa Guerrero MD^{1,2}, Catherine A. Flynn NP¹, Shayna Sarosiek MD^{1,2}, Steve P. Treon MD, PhD^{1,2}, Jorge J. Castillo MD^{1,2}

¹Dana-Farber Cancer Institute, Bing Center for Waldenström Macroglobulinemia, Boston, USA; ²Department of Medicine, Harvard Medical School, Boston, USA.

Abstract

Context: Waldenström macroglobulinemia (WM) is a rare type of B-cell lymphoma, with around 20% of patients having a family history of blood malignancies. However, most data about family history are derived from clinical databases with scarce information regarding clinical features, complications, and treatment outcomes among different family groups.

Objective: To determine the relationship between family history, presenting characteristics, complications, and treatment outcomes of patients with WM.

Design, Participants, and Setting: This retrospective study examines family history and clinical data from 1000 adult patients with a clinicopathological diagnosis of WM evaluated at our institution between 2000 and 2022. Patients were followed up until December 2023.

Main Outcome Measures: The primary outcome was to correlate clinical features at the time of diagnosis (sex, age, adenopathy, splenomegaly, hemoglobin, platelets, LDH, albumin, beta-2-microglobulin, IgM, light chain restriction, % bone marrow involvement, MYD88 and CXCR4 mutational status), complications at any time during the disease course (Bing-Neel syndrome, cryoglobulinemia, cold-agglutinin syndrome, malignant pleural effusions, renal involvement, DLBCL transformation, AL amyloidosis, and WM-attributed neuropathy), prevalence of family history (WM, other B-cell, non-B-cell, and sporadic) and treatment outcomes (treatment status, overall survival). Chi-square test and logistic regression models were fitted to evaluate relationships between variables. Cox proportional-hazard regression models were fitted to evaluate survival prognostic factors.

Results: The median follow-up time from diagnosis was 13 years (95% CI, 9.66-16.59). We found that compared with sporadic WM, patients with a family history of WM were more likely women (34% vs 50%; $P<0.01$). Patients with familial WM showed increased odds of developing Bing-Neel syndrome (OR 5.6; 95% CI, 2.1-14.4; $P<0.01$) and cryoglobulinemia (OR 3.1; 95% CI, 1.4-7.0; $P=0.01$) but less likely to develop neuropathy (OR 0.38; 95% CI, 0.2-0.8; $P=0.01$). In multivariate Cox regression analyses, no significant difference in excess mortality was detected in patients with family history of WM (HR, 1.1; 95% CI, 0.92-1.31; $P=0.3$).

Conclusion: Our study suggests that patients with a family history of WM are more likely women, have higher odds of cryoglobulinemia and Bing-Neel syndrome, and lower odds of neuropathy. However, no excess mortality was observed.

Keywords: IBCL, lymphoplasmacytic lymphoma, familial Waldenström macroglobulinemia, survival, Bing-Neel syndrome, family history