Risk factors in Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma

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A role for genetic factors in the causation of lymphoplasmacytic lymphoma/Waldenström macroglobulinemia (LPL/WM) is implicated based on prior findings from multiply affected families and smaller studies. Based on small numbers, certain infectious and autoimmune conditions have been associated with the risk of developing LPL/WM.

Based on 2144 LPL/WM patients (1539 WM [72%] and 605 LPL [28%]), 8279 matched controls, and linkable first-degree relatives of patients (n=6177) and controls (n =24,609), we calculated relative risks as measures of familial aggregation. In a follow-up study including 2470 LPL/WM patients, 9698 matched controls, and almost 30 000 first-degree relatives of either case patients or control subjects, we evaluated a wide range of autoimmune, infectious, allergic, and inflammatory conditions in relation to the risk of developing LPL/WM.

First-degree relatives of LPL/WM patients (vs. first-degree relatives of controls) had a 20-fold, 3.0-fold, 3.4-fold, and 5.0-fold increased risks of developing LPL/WM, non-Hodgkin lymphoma (NHL), chronic lymphocytic leukemia (CLL), and monoclonal gammopathy of undetermined significance (MGUS), respectively. In the second study, we found an increased risk of LPL/WM associated with a personal history of the following autoimmune diseases: systemic sclerosis, Sjögren syndrome, autoimmune hemolytic anemia, polymyalgia rheumatica, and giant cell arteritis (OR=2.9 to 24.2). An increased risk of LPL/WM was associated with a personal history of the following infectious diseases: pneumonia, septicemia, pyelonephritis, sinusitis, herpes zoster, and influenza (OR=1.4 to 3.4). Interestingly, an increased risk of LPL/WM was associated with a family history of the following autoimmune or infectious diseases: Sjögren syndrome (OR=5.0), autoimmune hemolytic anemia (OR=3.8), Guillain-Barré syndrome (OR=4.1), cytomegalovirus (OR=2.7), gingivitis and periodontitis (OR=1.9), and chronic prostatitis (OR=4.3).

The observed highly increased familial risks of developing LPL/WM, NHL, CLL, and MGUS support the operation of shared susceptibility genes that predispose to LPL/WM and other lymphoproliferative disorders. Also a personal history of certain immune-related and infectious conditions was strongly associated with increased risk of LPL/WM. The association of both personal and family history of Sjögren syndrome and autoimmune hemolytic anemia with risk of LPL/WM suggest shared susceptibility (genetic, environmental, or both).