Distinguishing IgM Monoclonal Gammopathy of Undetermined Significance (MGUS), Smoldering Waldenstrom's Macroglobulinemia (SWM), and Waldenstrom's Macroglobulinemia (WM)

Robert A. Kyle, MD

IgM MGUS is characterized by an IgM monoclonal protein < 3.0 g/dL, bone marrow containing fewer than 10% lymphoplasmacytic cells, absence of symptomatic anemia, lymphadenopathy, hepatosplenomegaly or hyperviscosity and no constitutional symptoms. In a long-term followup of 213 patients with IgM MGUS from Southeastern Minnesota, 29 developed lymphoma (N =17), WM (N = 6), AL amyloidosis (N = 3), and CLL (N = 3). The relative risk of progression was 15.9-fold higher than that expected. The risk of progression was 1.5 percent per year. The size of the serum M protein, serum albumin level, and hemoglobin value were all risk factors for progression. SWM is characterized by the presence of a serum IgM monoclonal protein $\geq$ 3.0 g/dL and/or $\geq$ 10% lymphoplasmacytic infiltration of the bone marrow. There must be no evidence of symptomatic anemia, lymphadenopathy, hepatosplenomegaly, hyperviscosity or constitutional symptoms. Forty-eight persons with SWM were identified at Mayo Clinic and followed for 292 person-years. The median duration of followup was 13.9 years. During that time, 33 persons progressed to symptomatic WM when only 0.004 were expected. Risk factors for progression were size of the serum M protein, degree of bone marrow lymphoplasmacytic infiltration, hemoglobin value, and the presence of reduction of uninvolved immunoglobulins. The risk of progression was 55% at 5 years (11% per year).