Long-term follow-up of IgM monoclonal gammopathy of undetermined significance (MGUS)

R.A. Kyle, M.D., T.M. Therneau, Ph.D., S.V. Rajkumar, M.D., J.R. Offord, B.S., D.R Larson, M.S., M.F. Plevak, B.S., L.J. Melton III, M.D.

Abstract

Purpose: To determine the outcome of patients who present with MGUS of the IgM class.

Methods: Two-hundred-fourteen patients with IgM MGUS were identified in southeastern Minnesota from 1960-1994. The primary end point was progression to lymphoma or a related disorder assessed by the Kaplan-Meier method.

Results: The 214 patients with IgM MGUS were followed for a total of 1,572 person-years (median 6.2; range 0-20.6 years per subject). Seventeen patients developed lymphoma (relative risk [RR] 14.7), and 6 developed Waldenström's macroglobulinemia (RR 259), while 3 developed primary amyloidosis (RR 16.1), and 3 have had chronic lymphocytic leukemia (RR 5.6). The relative risk of progression was 15-fold higher in the IgM MGUS patients as compared with the white population of the Iowa Surveillence, Epidemiology, and End-Results program. The cumulative incidence of progression was 10% at five years, 18% at ten years, and 24% at fifteen years. Multivariate analysis revealed that the size of the serum M-spike and the level of serum albumin at diagnosis were the only risk factors for progression to lymphoma or a related disorder. Age, gender, reduction of IgA and/or IgG immunoglobulins, presence or size of urine monoclonal protein, and size of liver were not prognostic features. The risk of progression to lymphoma or a related disorder at ten years after the diagnosis of MGUS was 14% for those with an initial monoclonal protein value of 0.5 g/dL or less, 26% with a value of 1.5 g/dL, 34% for 2.0 g/dL, and 41% for those with serum monoclonal protein above 2.5 g/dL. The risk of progression at ten years with an initial monoclonal protein value of 1.5 g/dL was 1.8 times the risk of progression with an initial value of 0.5 g/dL or less, while the risk of progression with a monoclonal protein value of 2.5 g/dL or more was 3.1 times the risk of progression with an initial value of 0.5 g/dL or less.

Conclusion: The risk of progression of MGUS of IgM type to lymphoma or related disorders averaged 1.5% per year throughout the period of observation.