

SMOLDERING WALDENSTRÖM MACROGLOBULINEMIA: FACTORS PREDICTING  
EVOLUTION TO SYMPTOMATIC DISEASE

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Waldenström Macroglobulinemia (WM) not requiring treatment for at least 12 months has been defined as smouldering WM (SWM). In SWM patients, factors predicting evolution to symptomatic disease are still undefined. Such risk factors were investigated in 27 SWM (20 males, 7 females) selected on the basis of the following criteria: (A)  $> 3$  g/dL IgM monoclonal component (MC), and/or (B)  $\geq 30\%$  bone marrow (BM) lymphoplasmacytoid infiltration, and/or (C) diffuse infiltration pattern on BM biopsy. Event-free survival curves were compared by means of log-rank test. Median MC concentration and BM infiltration were 1.8 g/dL (range, 0.2-4.5) and 40% (range, 0-90), respectively. The BM histological pattern was normal, interstitial and diffuse in 9%, 24% and 67% of patients, respectively. Mild anemia ( $10.8$  g/dL  $<$  hemoglobin  $\leq 12.5$  g/dL) was recorded in 22% of patients. At a median follow-up of 79 months (range, 14-204), 10 SWM patients (37%) showed progression to symptomatic disease, with a median interval from diagnosis of 46 months (range, 12-154). MC levels  $> 3$  g/dL were detected to predict progression to symptomatic disease ( $p < 0.0001$ ). Indeed, evolution was recorded in 4/4 (100%) of (A)+ patients [(A)+(B)-(C)-, 3/3; (A)+(B)+(C)+, 1/1] and in 6/23 (26%) of (A)- patients [(A)-(B)+(C)+, 5/10; (A)-(B)-(C)+, 1/3; (A)-(B)+(C)-, 0/10]. The presence of (B) and/or (C) criteria [with or without (A) criterion] did not correlate with SWM progression. A borderline predictive value for symptoms development was found for hemoglobin levels  $\leq 12.5$  g/dL ( $p = 0.07$ ). No other clinical or laboratory factor was significantly associated with the development of overt WM. In conclusion, for patients with SWM monoclonal IgM levels  $> 3$  g/dL and hemoglobin levels  $\leq 12.5$  gr/dL are likely to predict transformation into active disease requiring treatment.