[Abstract 20]

PROGNOSTIC FACTORS FOR TRANSFORMATION IN ASYMPTOMATIC IgM MONOCLONAL GAMMOPATHIES

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Introduction: Irrespective of the paraprotein size, asymptomatic IgM monoclonal gammopathies (aIgM-MG) are defined as: 1) monoclonal gammopathy of undetermined significance (IgM-MGUS) in the absence of morphological evidence of lymphoplasmacytic (LP) non Hodgkin's lymphoma (NHL) bone marrow (BM) infiltrate, or equivocal evidence of BM infiltrate without confirmatory immunophenotypic studies; or: 2) smouldering Waldenström's Macroglobulinemia (sWM) in the presence of unequivocal histopathological BM evidence of LP-NHL confirmed by immunophenotypic studies (SIgM+,CD5-,CD10-,CD19+,CD20+,CD22+,CD23-) (Semin Oncol 30:110-115, 2003). We evaluated the risk of transformation into symptomatic lymphoproliferative disease in aIgM-MGs as a whole, and in the two IgM-MGUS and sWM subgroups, defined according to above described criteria.
Patients and Methods: Three-hundred eighty-four patients with aIgM-MG diagnosed from November 1975 to January 2001 were studied. Cumulative probability of transformation was calculated by means of the Kaplan Meier estimator. Univariate and multivariate Cox models were used to identify possible predictors of evolution to symptomatic malignant disease.
Results: In aIgM-MG patients taken as a whole, the cumulative probability of transformation at 5 and 10 years was 8% (95%CI, 5-13%) and 29% (95%CI, 21-38%), respectively. After a median follow-up of 45 months (12-233), 45 aIgM-MGs (11.7%) evolved to symptomatic WM (n=41), NHL (n=2), IgM multiple myeloma (n=1), and primary amyloidosis (n=1). At univariate analysis, BM-LP infiltration, high erythrocyte sedimentation rate (ESR), hemoglobin (Hb) level, IgM size, and peripheral lymphocytosis, significantly correlated with evolution probability. At multivariate analysis, IgM size and peripheral lymphocytosis strongly correlated with prognosis, Hb level was associated with a trend for a higher progression risk. Analyzing a subset of 172 aIgM-MGs in which complete BM histopathological and immunophenotypic parameters were available, 138 were diagnosed as IgM-MGUS and 34 as sWM. Of 138 IgM-MGUS, 14 (10.1%) evolved to malignant lymphoproliferative disease (13 overt WM, 1 IgM MM) after a median of 75 months (12-117) from diagnosis. Of 34 sWM, 13 (38.2%) progressed to overt WM after a median of 55 months (13-154). EFS at 5 and 10 years was: 95% (95%CI, 87-98%) and 83% (95%CI, 71-90%), respectively, in IgM-MGUS; it was 77% (95%CI, 56-89%) and 42% (95%CI, 19-64%) in sWM (p=0.0001). IgM size, ESR level, degree of BM LP infiltration, and proportion of patients with polyclonal Ig reduction were significantly higher in sWM than in IgM-MGUS, while Hb level was significantly lower in sWM than in IgM-MGUS. In the latter group, at univariate analysis Hb level significantly correlated with transformation, while IgM size, detectable Bence-Jones proteinuria, and ESR where associated with only a trend for increased risk of evolution.
Conclusions: Among asymptomatic IgM-MGs, risk factors of evolution into symptomatic disease are IgM size, peripheral lymphocytosis, and Hb level. The population at high risk of evolution is represented by patients with sWM, a distinct entity with clear BM evidence of NHL and shorter EFS. In patients with IgM-MGUS, only Hb level significantly discriminates patients at higher risk of transformation.