Quantification of serum IgM kappa and IgM lambda in Patients with Waldenstrom's Macroglobulinemia.

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Introduction: Resolution of IgM monoclonal proteins (M-proteins) on serum protein electrophoresis (SPE) can make accurate quantification difficult. Specific polyclonal antibodies which recognise epitopes spanning the junction of the heavy and light chains of the individual immunoglobulin isotypes have been produced. These have been used successfully in the identification and monitoring of IgA and IgG M-proteins in myeloma patients. Here we describe the use of the automated nephelometric assays to quantify serum concentrations of IgMκ and IgMλ and the use of IgMκ / IgMλ ratios to identify IgM M-proteins.

Patients and Methods: Retrospective sera from 39 patients with IgM M-proteins (25 IgMκ, 13 IgMλ and 1 patient with IgM restriction but no identifiable light chain) identified between 17/3/1989 and 22/4/2008 were included in this study (31 WM, 4 IgM monoclonal gammopathy of undetermined significance (MGUS), 2 symptomatic MGUS (Neuropathy) and 2 mantle cell lymphoma). Analysis of IgMκ and IgMλ was performed on a Siemens Dade-Behring BNTII nephelometer and results compared previously measured serum markers and International Prognostic Scoring System (IPSS).

Results: Abnormal IgMκ / IgMλ ratios were reported in 30/31 WM, 5/6 MGUS and 1/2 mantle cell lymphoma patient sera. In the one WM patients with a normal IgMκ / IgMλ ratio at presentation, total IgM levels were within the normal range (1.9g/L) and the patient did not require treatment. There was a good correlation between summated IgMκ + IgMλ and total IgM (r=0.832 p<0.0001), although in 12 patients there was considerable disagreement between total IgM (range 12.9-80.4) and summated IgMκ + IgMλ (range 22.2-150.8, p>0.01). Theses 12 patients presented polyclonal hypogammaglobulinemia (with regard to their IgG and IgA levels). Median levels of the IgMκ / IgMλ ratios (expressed as IgMκ / IgMλ or IgMλ / IgMκ) were 90.88 (range 1.91-1000) in WM v 17.65 (range 1.08-34.57) in IgM MGUS (p=0.06). Median IgMκ / IgMλ ratio was higher in WM patients requiring treatment (n=24) at presentation than in patients not (n=7)
requiring treatment (185.7 v 13.45 p=0.023) (figure). IgMκ / IgMλ ratio correlated weakly with bone marrow infiltration (r= 0.373, p=0.029) but strongly with overall IPSS (r=0.593, p=0.001). IPSS separated patients into 3 prognostic arms with respect to overall survival (OS, p=0.019), using a simple algorithm (β2M>5 and a IgMκ / IgMλ ratio >100 or < 0.1) 3 prognostic arms were similarly identified with respect to OS (p<0.0001). The patients identified in the highest risk group for each risk model had markedly different 50% survival times (1077d for IPSS compared to 423d for β2M+ IgMκ / IgMλ ratio).

Conclusions: Analysis of IgMκ / IgMλ correlated with bone marrow infiltration and IPSS. A risk stratification model using β2M and extreme IgMκ / IgMλ ratios identified WM patients with a more aggressive disease. This early study identifies a potential utility in measuring IgMκ / IgMλ ratio in WM patients although larger studies are required to validate their utility.