

Novel nephelometric assays give a sensitive measure of residual disease in multiple myeloma

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Introduction

Here we report preliminary results using novel immunoassays to determine the serum IgAk / IgA λ or IgGk / IgG λ ratios of myeloma patients and use these ratios for tumour monitoring. Normal ranges for the IgAk / IgA λ and IgGk / IgG λ ratios were derived from 120 blood donor sera.

Methods

5 IgA and 7 IgG patients were analysed throughout the course of their disease and results compared with conventional assessments. In 2/5 IgA and 1/7 IgG patients the ratios gave a more sensitive indication of residual disease.

Results

In one IgA λ patient, densitometric measurement of the monoclonal protein by serum protein electrophoresis (SPE) was impossible throughout as it was hidden by other proteins. The IgAk / IgA λ ratio remained abnormal 518 days after immunofixation (IFE) became negative. In a IgAk patient, utilising the IgAk / IgA λ ratio indicated progression 596 days earlier than reported by SPE or IFE. Similarly, in an IgG λ patient, disease progression was detected 406 days earlier. After chemotherapy (CVAMP) in this patient, the total IgG level fell and a second response was reported. However, during this period the IgGk / IgG λ ratio remained unchanged indicating that there was no selective tumour kill. In addition, 26 IgA (15 IgAk / 11 IgA λ) and 19 IgG (10 IgGk / 9 IgG λ) multiple myeloma patient samples were analysed at presentation by either IgAk and IgA λ or IgGk and IgG λ specific assays in all cases the correct monoclonal immunoglobulin was reported.

Conclusion

This preliminary data indicates it is possible to type and monitor monoclonal immunoglobulins by quantifying the immunoglobulin κ / λ ratios. Measuring the alternate immunoglobulin light chain levels gives information regarding the level of immunoparesis and makes the immunoglobulin κ / λ ratios a more sensitive marker of residual disease.

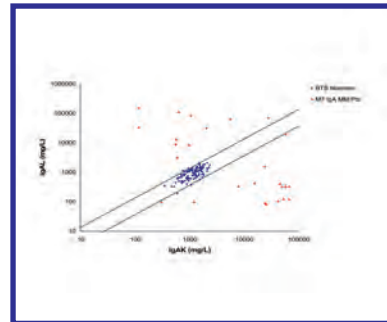


Figure1: Plot of IgA κ v IgA λ for 121 blood donor sera and 26 presentation sera from the MRC Myeloma VII trial. The parallel lines indicate the 95% range for the IgA κ / IgA λ ratio.

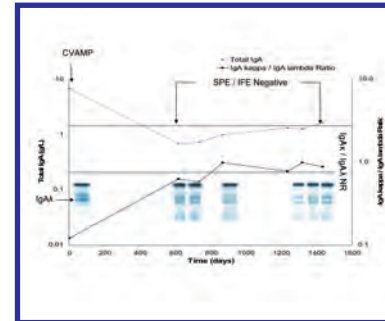


Figure2: Serial analysis of IgA patient's sera comparing total IgA and the IgAk / IgA λ ratio, accurate quantification of the IgA monoclonal protein by SPE and densitometry was impossible throughout the course of the disease.

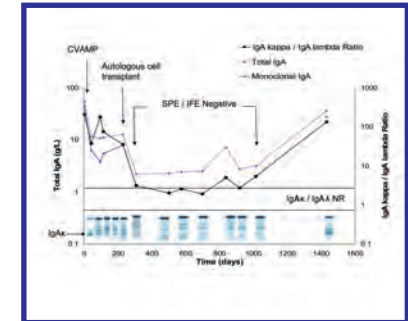


Figure3: Serial analysis of IgA patient's sera comparing monoclonal IgA from SPE densitometry, total IgA and the IgAk / IgA λ ratio. The ratio became abnormal before a band was quantifiable by SPE.

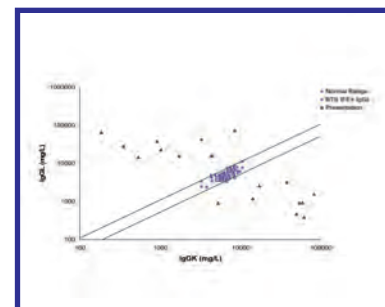


Figure4: Plot of IgG κ v IgG λ for 108 blood donor sera and 19 presentation sera from MRC the Myeloma VII trial. The parallel lines indicate the 95% range for the IgG κ / IgG λ ratio. One normal blood donor sera had an abnormal IgG κ / IgG λ ratio and was found to have monoclonal IgG λ by IFE, this serum is labelled as MGUS.

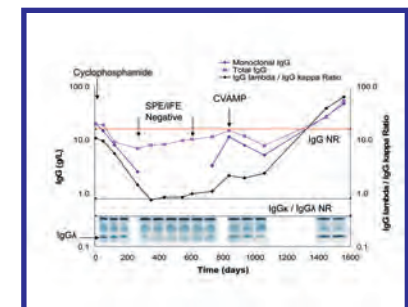


Figure5: Serial analysis of IgG patient's sera comparing monoclonal IgG from SPE densitometry, total IgG and the IgG κ / IgG λ ratio. At relapse the ratio became abnormal before a band was quantifiable by SPE. During the treatment for relapse, a fall in total and monoclonal IgG was apparent, but the ratio indicated no selective tumour kill.