

Abnormal serum free light chain ratios are associated with poor survival in patients with chronic lymphocytic leukaemia

G Pratt¹, S Harding², R Holder³, C Fegan⁴, C Pepper⁴, D Oscier⁵, G Mead² ¹CRUK Institute for Cancer Studies, University of Birmingham, UK ²Binding Site Ltd, Birmingham, UK ³The Department of Primary Care General Practice, University of Birmingham, UK ⁴Department of Haematology, Cardiff University, UK, ⁵Department of Haematology, Royal Bournemouth Hospital, UK

Introduction

The measurement of immunoglobulin free light chains (FLC) in serum can be used as an aid in the management of a number of plasma cell dyscrasias. The presence of an abnormal FLC ratio has also been reported to be prognostic in monoclonal gammopathy of uncertain significance, solitary plasmacytoma of the bone, multiple myeloma, Waldenström's macroglobulinaemia and AL amyloidosis. The incidence of abnormal FLC in other lymphoid malignancies including chronic lymphocytic leukaemia (CLL) is unclear with only one published report which found 8/18 CLL patients with an abnormal FLC. There have been no studies correlating FLC with other biological variables and clinical outcomes in CLL or lymphoma.

Method and Results

This was a retrospective study that analysed serum FLC results measured at varying time points in 226 CLL patients (183 Stage A, 18 Stage B, 16 Stage C, 9 unknown, mean age 74, male:female ratio 2.2:1) treated at 3 separate hospitals in the UK and correlated serum FLC with biological and clinical markers. Using Kaplan Meier survival hazards, abnormal FLC ratio was a significant indicator of poor survival ($n=226$, Log rank $p=0.001$) and also time to first treatment. Using Cox regression forward, stepwise analysis ($n=142$ with complete data sets) we analysed stage, CD38, Zap-70, mutation status, FLC ratio, β_2M and age. The analysis indicated four independent prognostic variables namely Zap-70 ($p<0.001$), β_2M ($p=0.002$), mutation status ($p=0.003$) and FLC ratio ($p=0.009$).

Conclusion

We conclude that an abnormal free light chain ratio contributes significantly and independently to the prediction of a worse outcome. Serum FLC at diagnosis needs to be studied prospectively in CLL patients and the biological rationale for its adverse impact needs investigating.

