Use of monoclonal indicators in the progression of IgA monoclonal gammopathy undeterminated significance, to multiple myeloma

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INTRODUCTION: The monoclonal gammopathy of undetermined significance (MGUS) is one of the more frequent premalignant disorders affecting around 3% of population over 50 years old.

Monoclonal protein isotype is a predictive factor of independent progression. IgA MGUS shows a risk of progression to multiple myeloma (MM) in 20 years of 21% (Rajkumar et al).

Currently, the use of new monoclonal indicators: free light chains (FLCs) and heavy/light chain pairs (Hevylite®) can provide more information to detect patients able to develop the malignant illness. At the last IMWG consensus a FLC ratio of at least 100 is a progression predictor.

MATERIAL AND METHODS: 94 diagnosed IgA MGUS patients, without organs' affection related to MM (CRAB), were assessed. Routine biochemistry and haematology test were performed, total immunoglobulins (nephelometry. Siemens) electrophoretic and immunofixation (SEBIA). Free Light Chain (Freelite®) and Hevylite® IgA (The Binding Site). A patient progression from MGUS IgA to asymptomatic MM is showed.

RESULTS: Patients' cohort age median was 72. IgA total median was 1200 mg/dL. 10 patients showed immunoparesis of non-involved isotypes (IgG e IgM) (IgG 670 mg/L and IgM 27 mg/L) and 15 patients immunoparesis of Hevylite non-involved pair. 20% of patients showed the involved FLC 100 mg/L and involved and non-involved chain difference (dFLC) 100.

The bone marrow test was no mandatory, it was only made on the evolved patient to asymptomatic MM.

A 79 years old patient diagnosed with MGUS IgAκ in 2012 with PM: 0.74 g/dL, κ/λ: 13,97, dFLC: 38,25, suppression of the non-involved pair IgAλ: 0,23 mg/L (0,36-1,98), and immunoparesis of the non-involved isotypes, IgG 433 mg/dL, IgM 23,6 mg/dL. Since July 2012, she presents FLCκ 100, dFLC 100, PM 1,5 g/dL, without CRAB. A bone series was made in January 2015 and a magnetic resonance in June 2015 without injuries compatible with MM. In June 2015 bone marrow showed 18% of plasmatic cells and the histocompatibility test compatible with evolved MGUS to asymptomatic MM.

CONCLUSIONS: MGUS precedes MM diagnosis. The application of IMWG new protocols allows to select patients with a higher evolution risks who, although not treated, will be followed-up more carefully by the haematologist.

From the biochemical point of view, the patient presented monoclonal indicators compatibles with progression since July 2012, having been diagnosed with asymptomatic MM in June 2015.

Hevylite® ratio confirms the monoclonality and the decreased in the concentration of the non-involved pair would show a worse prognosis for the patient, marking the risk of progression.

FLCs and Hevylite® jointly used provide a prognosis information, selecting patients with a higher risks of progression to MM and may objectify when to make a bone marrow test.

Bibliography: International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma. S Vincent Rajkumar et al. Lancet Oncol 2014; 15:e538-48.

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