

IMMUNOPHENOTYPIC ANALYSIS OF WALDESTRÖM'S MACROGLOBULINEMIA

J.F. San Miguel, MB. Vidriales, G. Mateo, E. Ocio, F. Sánchez-Guijo, M.L. Sánchez, L. Escribano, A. Báñez, M.J. Moro, J. Hernández, C. Aguilera, R. Cuello, R. López, J. Portero, A. Orfao.

Immunophenotyping has become an essential tool for diagnosis of many haematological malignancies such as acute leukemias and non-Hodgkin lymphomas. By contrast, for diagnosis of Waldenström's Macroglobulinemia (WM) immunophenotyping is used only occasionally. From a series of 150 patients with a IgM monoclonal gammopathy we have selected 70 cases who fulfill the following criteria for WM: 1) morphological lymphoplasmocytoid BM infiltration (>20%); 2) IgM paraprotein (>10 g/l; median 30 g/l) and 3) absence of features of other lymphoma types. Immunophenotypic analysis was based on the use of the triple or quadruple monoclonal antibodies combinations which included the following antigens: CD5, CD10, CD11b, CD11c, CD19, CD20, CD21, CD22, CD23, CD24, CD25, CD27, CD38, CD56, CD45, CD45RA, CD45RO, CD138, HLA-DR, FMC7, bcl-2, μ Ig and the surface and cytoplasmic expression of κ Ig and λ Ig. In order to increase the sensitivity of the analysis of antigen expression, selected CD19⁺CD20⁺ B-cells were targeted. In addition, we have also explored the antigenic characteristics of both the plasma cell (PC) and mast cell (MC) compartments present in the BM from WM patients. Clonal lymphocytes from WM were characterized by the constant expression of pan-B markers (CD19, CD20, CD22) together with sIg, predominantly kappa (4:1, κ : λ ratio). In addition, a high proportion of cases were positive for FMC7 (75%) and CD25 (> 90%), but in contrast to "hairy cell leukemia", these lymphocytes were always negative for CD103. CD11c and CD23 were negative in most malignant B-cells in all cases, although small subset of dim-positive cells (< 10%) was frequently present. CD10 was also absent in all WM patients which may help in differential diagnosis with some forms of CD10⁺ NHL (i.e. follicular) with bone marrow involvement. Less than one fifth of patients were positive for CD5, while CD38, BCL-2 and HLA-DR were generally present in most malignant cells. In 10% of the cases, two different lymphoid subsets (defined by the presence or absence of antigens such as CD5, CD23, CD11c and FMC7) co-existed. In 13 WM patients, we analyzed the phenotype of plasma cells (PC) and mast cells (MC). In most patients (85%) the number of PC was within the normal range (median: 0.36%, range: 0.15% - 0.58%). The antigenic profile of these cells was CD38⁺CD19⁺CD56⁺CD45^{++ or +++}CD20^{+/-}. Three cases showed aberrant expression for CD5, CD22 or FMC7. The FSC/SSC characteristics of these cells ranged from those of conventional PC to lymphoplasmocytes. Finally, the number of MC were significantly higher (0.058 +/- 0.13) as compared to normal BM (0.019 +/- 0.02) (p < 0.01), although they were immunophenotypically normal (CD117⁺CD2⁻CD25⁻).