Session V: Prognostic, Predictive and Response Markers in WM

Abstract 126

Presenter: J. Feuillard

Plasma cell differentiation in indolent lymphomas originated from marginal zones. Jean Feuillard, Centre Hospitalier Universitaire (CHU) Dupuytren and Faculté de Médecine, Université de Limoges, FRANCE.

Marginal zone (MZ) of secondary lymphoid organs is a heterogeneous territory in terms of cellular composition. Initially ascribed to T-dependant memory B-cells, MZ also comprises at least two other B cell subsets: naive B lymphocytes devoted to the response to T-dependent antigens and B lymphocytes originating from T-independent responses. Apart MALT lymphomas, indolent lymphomas supposed to derive from MZ (MZL) are those from spleen (S-MZL) and lymph nodes (N-MZL), as well as controversial lymphoplasmacytic lymphomas (LPL) and their clinical variant, Waldenström's macroglobulinemia. Overlaps exist between these 3 different entities, due to absence of specific markers, to frequent IgM monoclonal component in the serum and to partial engagement of tumour cell in plasma cell differentiation, the latter being probably a poor prognosis marker. Chronic antigen stimulation is very likely to play a role in MZLs of secondary lymphoid organs. Auto-immune haemolytic anemia or thrombopenia is found in 2% to 16% of patients. There is an association between Hepatitis C virus (HCV) chronic infection and SMZL, supposedly those with circulating villous lymphocytes. Monoclonal auto-antibodies specific for coagulation factors or nervous system proteins are frequent in LPL/WM. The biased usage of *IGHV* gene segment (*IGHV1-2*04* in SMZL, *IGHV4-34* in NMZL and *IGHV3-23* in LPL/WM and WM) is in favour of an antigen selection driven process. These observations indicate that MZL cells express BCR of different specificities, according to their histological localisation and/or their Ag exposure histories. Classical cytogenetics is not discriminant: some cytogenetic abnormalities are shared by MALT lymphomas and the other MZL (trisomies 3, 18, and 12, especially when associated). Other seem more specific such del7q described as recurrent in S-MZL, del6q21-23 although debated in LPL and trisomy 4 in WM. Thus, at the cytogenetic level, MZLs of secondary lymphoid organs seem to resemble CLL rather than MALT lymphomas, being associated with genetic imbalances rather than with reciprocal translocations. It suggests that different mechanisms of transformation occur in MZLs of secondary lymphoid organs or LPL/WM and MALT lymphomas. To better understand these lymphomas, we have developed a multicentric study on 310 tumours. Immunophenotype had been studied for 271 cases, 251 being included in a Tissue-Micro-Array. RNA and DNA have been extracted from 147 and 140 cases respectively. We will present the advancement of our work regarding the morphological characterisation, transcriptome analysis, IgVH gene sequencing, and plasma cell differentiation. We will focus on the resemblance and differences between LPL/WM and MZLs of secondary lymphoid organs. Results will be discussed in the light of the physiology of the B-lymphocyte and of the normal plasma cell differentiation.