[Abstract 13]

CLINICOPATHOLOGICAL FEATURES OF WALDENSTRÖM'S MACROGLOBULINEMIA AND MARGINAL ZONE LYMPHOMAS : ARE THEY DISTINCT OR A SINGLE ENTITY?

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Waldenström's macroglobulinemia (WM) is considered in the WHO classification of lymphomas as a clinical syndrome secondary to monoclonal IgM secretion, mainly observed in patients with lymphoplasmacytic lymphoma (LPL) and occasionally with other small B-cell lymphomas. Some authors consider it as a rare distinct lymphoproliferative disorder with primary bone marrow infiltration and IgM monoclonal gammapathy. As LPL shares important morphological and immunophenotypic overlap with marginal zone B-cell lymphomas (MZL), especially when those cases show a plasmacytic differentiation, it remains unclear if they constitute unique or distinct entities. Both diseases are composed of lymphocytes, lymphoplasmacytoid cells and plasma cells with a sIgM+ sIgD+/- cIgM+ CD19+ CD20+ CD27+/- CD5- CD10- CD23- phenotype, without a specific marker. The t(9;14) PAX5-IgH translocation reported in cases of LPL without IgM spike and translocations involving the IgH locus were not found in recent series of LPL/WM. The association of WM to 6q deletions recently described must be confirmed, this anomaly being a frequent secondary alteration in other B-cell lymphomas. Molecular Ig VH gene analysis suggests that WM arise from a mature IgM+ B-cell transformed after completion of somatic mutations but prior to isotype switch events. The three types of MZL (extranodal, nodal and splenic) listed in the WHO classification are distinct entities displaying common morphological, immunophenotypic and genetic (trisomies 3 and 18) characteristics. Extranodal MZL (MALT lymphoma) is well defined, with three specific translocations, t(11;18) API2-MALT1, t(1;14) IgH-BCL10 and t(14 ;18) IgH-MALT1, leading to the activation of NF-κB. This frequent indolent lymphoma is clearly distinct from LPL/WM, although bone marrow infiltration and IgM paraprotein are not rare. Splenic (S) and primary nodal (N) MZL are less frequent and incompletely characterized. A pure monocytoid cytology is rare and plasmacytoid/plasmacytic differentiation more usual. In both diseases, autoimmune manifestations and a monoclonal component are frequent. Bone marrow involvement, constant in SMZL, is present in 60% of nodal MZL. Few genetic alterations have been reported, except 7q deletions and t(7q21;N) leading to the overexpression of CDK6 in SMZL and rare controversial t(11,14) with deregulation of cyclinD1; del 6q and del 17p appear linked to clinical progression. Their clinical outcome is different: SMZL is indolent with a slow progression, while NMZL (often large cell-rich) is more aggressive and disseminated, with a rapid progression but a long survival. Molecular IgVH gene analysis has confirmed this heterogeneity, particularly within the group of SMZL, with mutated and unmutated cases, consistent with a derivation from the 2 types of normal SMZ B-cells, including naive and memory B-cells. Further studies are needed to clarify the pathogenesis of these MZL and their relationship with WM, which might be a primary medullar subtype of mutated SMZL.