CLINICO-PATHOLOGICAL STUDY OF WALDENSTROM MACROGLOBULINEMIA IN FAR-EAST-ASIA

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(Background) Deletion 6q including loss of B-lymphocyte-induced maturation protein1 (BLIMP1) was found in 40-55% of WM in the US and European countries. BLIMP1 gene is reported to play an important role in differentiation of B-cells to plasma cells (PC), and loss of BLIMP1 is considered as one of the important oncogenesis mechanisms in Waldenstrom Macroglobulinemia (WM). Some of the investigators found correlation between PC percentage (%) in bone marrow (BM) and serum IgM level in WM. On the other hand, relation between loss of BLIMP1 and PC % in BM, and other clinicopathologic factors have not been fully investigated. Additionally, reports of WM from Far-East-Asia have been limited so far. (Aims) We conducted multi-center retrospective analysis to clarify the following points: 1) Whether the loss of BLIMP1 affects PC percentage in BM 2) Clinical, pathologic, and cytogenetic features of WM in Far-East-Asia (Methods) Newly diagnosed WM cases from January 2000 to March 2014 in Disaster Medical Center, Tokyo Women’s Medical University Hospital, and January 2000 to December 2012 in Seoul National University Hospital were enrolled in this study. The institutional review board approval was obtained from each hospital. Clinical data was obtained from the medical charts, including clinical symptoms, laboratory, and radiological findings. Pathologic review was also performed including PC % in BM, and all cases were IgM-WM. Cytogenetic aberration was obtained by G-banding method and FISH analysis using A20/BLIMP-1/SHGC-79576 Three Color Probe (Cancer Genetics Italia TM). Statistical analysis including relation between the existence of BLIMP1 and clinical factors were performed. (Results) 46 clinical data were obtained. Median age was 69 years old (40-88) and male/female was 34/12. Median serum IgM level and M-protein level was 2,277 mg/dL (317-6,810) and 2.595 g/dL (0.55-8.91). The proportion of low, intermediate, and high risk group according to International prognostic scoring system for WM was 9, 36, and 55%,
respectively. Hepatomegaly, splenomegaly, and B-symptom were recognized in 23.8, 23.8, and 29.4%, respectively. Osteolytic bone lesion including punched out lesion in skull was recognized in 13/35 (37.1%), and lymphadenopathy mostly in the form of retroperitoneal lymph node swelling like soft tissue mass was found in 21/42 (50%). 34 bone marrow smears were reviewed. Median PC %, lymphoplasmacytic cells %, small lymphocyte %, and total neoplastic cell % was 2.8% (0-32.9), 3.5% (0-84.6), 32% (0-93.2), and 45.2% (6.2-96.2). The incidence of loss of del 6q was 2/40 (5%) by G-banding, and 11/37 (29.7%) by FISH. All cases with loss of BLIMP1 had loss of A20 by FISH analysis. The correlation between serum IgM level and PC % was recognized (r=0.57 (p=0.001)). Serum IgM level was higher in cases with loss of BLIMP1 (mean: 4,027 mg/dL) than those without loss of BLIMP1 (mean: 2,198 mg/dL, p=0.02). Creatinine clearance was worse in cases without loss of BLIMP1 group (P=0.02). On the other hand, no correlation was recognized with or without loss of BLIMP1 and pathologic factors. The only factor that has correlation with osteolytic bone lesion was serum compensated calcium level (P=0.06). (Conclusion) Our clinicopathologic study showed no significant correlation between PC % in BM and the presence of BLIMP1. However, serum IgM level was significantly different among cases with and without BLIMP1. We found the incidence of del 6q is lower, and that of osteolytic bone lesion, and lymphadenopathy in retroperitoneum was higher than the report in US and European countries. Therefore, Asian cases of WM might be recognized as a variant of WM.