IMMUNOPHENOTYPIC AND MOLECULAR CHARACTERISTICS OF B-CELL LYMPHOMAS WITH LEUKEMIC PHASE, VILLOUS MORPHOLOGY AND SPLENOMEGALY

Yanitsa Davidkova, Gueorgui Balatzenko, Rositsa Vladimirova, Maria Muhtarova, Tihomir Dikov, Valentina Madzharova, Milan Jagurinoski, Branimir Spasov, Margarita Guenova

National Specialised Hospital for Active Treatment of Hematological Diseases, Sofia

The spectrum of leukemic lymphomas with villous morphology and mature B-cell phenotype of the malignant population, as well as splenomegaly in the clinical presentation represent a differential diagnostic problem that requires a complex approach.

The aim of the study was to determine the role of immunophenotypic and molecular biomarkers that complement the clinical and laboratory parameters in the diagnosis of B-cell leukemic lymphomas with villous morphology and splenomegaly.

Materials and methods: In total 91 patients were included in the studyq including 64 patients with classic hairy cell leukemia (cHCL), 9 with variant (v)HCL and 18 with splenic marginal zone lymphomas (SMZL), diagnosed from 2005 to 2018 at the National Specialized Hospital for Active Treatment of Hematological Diseases.

Results: The analysis demonstrated significant differences between the nosologigal categories. The mean age of patients with cHCL (53.3 years) was significantly lower than that of the patients with vHCL (69.8 years) and SMZL (65 years) ($p < 0.001$). Male: female ratio of the patients with cHCL was 4.8:1 (53 men, 11 women) as opposed to vHCL (0.8: 1) and SMZL (0.8: 1) ($p = 0.001$). The mean leukocyte count in cHCL (4.4 $x10^9$/l) was significantly lower than in patients with SMZL (27.5 $x10^9$/l) and vHCL (39 $x10^9$/l) ($p < 0.001$). Substantial differences in the immunophenotype were also found. The hairy cells in cHCL were 100% positive for CD103, CD25 and CD11c, 97% for CD200 and 95% for CD305. Although patients with vHCL were also positive in 100% for CD103 and CD11c, and in 83% for CD305, the expression of CD200 was positive in only 63% and CD25 in only one patient ($p < 0.001$). Classical and vHCL also differed in CD31 and CD27. Patients with SMZL were characterized by a significantly lower prevalence of CD31 (5%), while CD27 was positive in 77% of the cases ($p = 0.010$). The assessment of CD185 showed complete absence in vHCL compared to 57.1% and 93% in cHCL and SMZL ($p = 0.001$). The differences in the phenotypic characteristics between cHCL and SMZL were more pronounced - CD103 was negative in all cases with SMZL, and CD11c (29%), CD200 (41%), CD25 (54.5%) and CD305 (70%) were marked in significantly fewer cases ($p<0.05$). CD81, which was found in 100% of patients with vHCL and SMZL, was positive in only 41.4% of cHCL ($p < 0.001$). Additionally, the detection of BRAF V600E mutation clearly distinguished patients with cHCL, while the mutation was not found in vHCL and SMZL ($p < 0.001$).

Conclusion: The integrated clinical and laboratory approach allows reliable distinction of different nosological entities and thus - selection of optimal therapy.