Abstract

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Chronic lymphocytic leukemia (CLL) is a disease characterized by clonal proliferation of B-lymphocytes. CLL is a lymphoproliferative disorder with a number of defined risk factors, but its etiopathogenesis remains unresolved to some degree. Over the past 10-15 years, there have been several studies that primarily suggest a genetic predisposition to the disease. The influence of external factors on the etiology of CLL has not been demonstrated. There is also a defined asymptomatic condition associated with CLL called monoclonal B-lymphocytosis, which is often referred to as a precursor of CLL.

Immunophenotyping of lymphocytes by flow cytometry was performed in subjects of the control group (100 subjects) and the CLL/MBL group (patients diagnosed with CLL or MBL, 50 subjects). All subjects in the control and CLL/MBL groups were screened for selected genetic polymorphisms (rs17483466, rs735665, rs7176508, rs872071, rs13397985) that have been associated with the occurrence of CLL and MBL in other studies. The aim of this work was to compare the representation of the genotypes in the control and CLL/MBL groups and to evaluate the association of the tested single nucleotide polymorphisms with CLL, MBL disease.

Patients in the CLL/MBL group were diagnosed with CLL (37 cases) based on the results of blood counts and peripheral blood flow cytometry analyses, and with MBL (13 cases) if numerical (low number of clonal lymphocytes) or clinical criteria were not met. Patients diagnosed with MBL were divided into a group with low or high numbers of circulating clonal B-lymphocytes. The resulting immunophenotype was the same in all patients: typical of clonal CLL cells (CD5+ CD23+ $CD20^{dim}$). One of the 5 polymorphisms studied, rs735665, was found to be significant for increased risk of both CLL and MBL disease ($p = 0.007$). A trend towards increased risk for CLL or MBL disease was observed depending on the number of risk alleles in the genotype with a higher proportion of risk alleles in the polymorphisms (rs17483466, rs735665, rs7176508, rs13397985).

A whole spectrum of factors comes into play in the pathogenesis of both CLL and MBL disease. A demonstrably older age of the individual is one risk factor. Another important factor is family history – in particular, first-generation relatives of patients with CLL have a higher risk of developing CLL (the so-called familial form) than those without a family history. Associated with this is a genetic predisposition to CLL/MBL, i.e. changes at the chromosomal and molecular level.