Abstract

Malignant lymphoproliferative disorders include highly heterogeneous entities, i.e. lymphomas (Non-Hodgkin – NHL, as well Hodgkin´s lymphoma), lymphoid leukemias, multiple myeloma and others. As currently many chromosomal aberrations with diagnostic and prognostic significance are known, molecular cytogenetic analyses of tumor cell genome has become a substantial examination also in lymphoproliferative disorders. This thesis focuses primarily on chronic lymphocytic leukemia (CLL), which is one of the mature B-cell neoplasms and represents the most common type of leukemia. We analyzed four most frequently found aberrations (13q14 deletion, *ATM* and *TP53* gene deletion, and trisomy 12) by fluorescence *in situ* hybridization (FISH) and also *IgH* gene aberrations in some patients. We compared the findings with other factors and clinical characteristics.

This work shows that the conventional G-banding is analysis relatively little relevant. FISH was more effective in detecting aberrations in CLL. Although none of the four aforementioned changes is specific to CLL, the prognostic impact is significant, particularly that of *TP53* deletion. Next, detection of some *IgH* gene translocations is essential in differential diagnosis of CLL and other NHL (follicular, mantle cell, diffuse large B cell, Burkitt´s lymphomas).

We attempted to confirm the impact of individual CLL aberrations. Our results verified the prognostic relevance of hierarchical categories. According to overall survival data, the best outcome was found in normal finding and 13q deletion subgroups, whereas it was intermediate in trisomy 12 and an inferior in *ATM* and *TP53* gene deletion categories.

The major part of the thesis deals with clonal evolution (CE) in CLL, studied in a cohort of 292 of patients subsequently analyzed by FISH. We investigated which risk factors relate to each type of CE and their influence on survival. In case of CE 13q and CE 11q, the only factor was found, namely the dutation of follow-up. Prognostically the worst possible CE, the occurrence of *TP53* deletion, significantly shortened overall survival and was associated with unmutated *IgVH* gene status, positive of CD38 and ZAP-70 expression, and previous chemotherapy.

The Ph.D. thesis comprises comments on own published papers directly related to objectives as well as research results yet unpublished.

Key words: cytogenetic aberrations, FISH, CLL, CE, NHL.