Analysis of cell cycle in B-cell lymphomas

Abstract

Introduction: In malignant lymphomas, the cell kinetics is related to the histological grade as well as to the clinical behavior. The aim of the study was to investigate the cell proliferation (MFI CD 71; PI) and the expression of important regulators of the cell cycle, i.e. cyclin D1, p21, p27 and p53, in patients with B cell non-Hodgkin's lymphoma (B-NHL). The expression of these proteins is often deregulated and the quantification of these proteins might be helpful for the specification of the diagnosis and prognostication of patients.

Methods: The proliferative activity was analysed in 112 patients by flow cytometry through assessment of the amount of DNA, proliferation index (PI), and median fluorescence intensity of transferrin receptor CD 71 (MFI): Further, cyclin D1, p21, p27 and p53 were analyzed by means of flow cytometry (n = 80) and western blot (n = 61).

Results: Cell proliferation activity increased according to the increasing malignancy of lymphomas [PI ($p < 0.0001$), MFI CD71 ($p < 0.0075$)]. Increased proliferative activity was detected in B-NHL with aneuploid DNA [PI ($p < 0.0001$), MFI CD71 ($p < 0.0016$)]. I demonstrated that the assessment of MFI CD71 and PI is a suitable method for the distinguishing between the low-grade follicular lymphomas (FLs) and high-grade B-NHLs with identical immunophenotype (Burkitt lymphoma, diffuse large B cell lymphomas, FL high). The overexpression of cyclin D1 detected by these methods was typically present in mantle cell lymphomas (MCLs), in contrast to the other non-MCL lymphomas ($p < 0.0001$). No statistically significant association between the p21 protein expression and the proliferation, the type or grade of the specific B-NHL was disclosed. The inverse correlation between the proliferative activity and the p27 expression was evident in the data. I demonstrated high level of this inhibitor in low-grade lymphomas with low proliferative activity ($p < 0.0002$) in contrast to high-grade lymphomas. I detected an overexpression of p53 especially in aggressive lymphomas, which are accompanied with chromosomal aberrations and low level of p27 expression.

Conclusions: The obtained results pointed out the importance of the analysis of the proliferative activity and its correlation to the grade of B-NHL. They confirmed the superior sensitivity of flow cytometry and WB as methods for cyclin D1 detection and therefore they are suitable for diagnostic evaluation of MCL. The results prove prognostic value of the p27 and p53 proteins assessment, on the other hand, they don't show clear evidence for a potential use of p21 as a prognostic marker.

Keywords: B-NHL, cell cycle, cell proliferation, cyclin D1, p21, p27, p53