

Down-regulation of p27 Is Associated with Malignant Transformation and Aggressive Phenotype of Cervical Neoplasms

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摘要

Abstract

Objectives. p27(Kip1) (p27) is a member of the cyclin-dependent kinase inhibitor family. The level of p27 protein expression decreases during tumor development and progression in some epithelial tumors. To identify the potential implications of the p27 gene in the development of cervical carcinoma and explore the clinical importance of change in gene expression, we assessed the level of p27 protein in precancerous lesions and carcinomas of the cervix. **Methods.** In our study, 20 low-grade squamous intraepithelial lesions (LSIL), 35 high-grade squamous intraepithelial lesions (HSIL), 12 microinvasive carcinomas, and 103 invasive carcinomas were evaluated. The expression of p27 was studied by immunohistochemistry using a monoclonal antibody specific for the protein. **Results.** p27 was expressed in all samples of normal epithelium, LSIL, and HSIL, and the mean values of expression were 55.1, 52.8, and 45.4%, respectively. Conversely, the expression of p27 was significantly reduced in microinvasive (15.9%) and invasive carcinomas (11.2%). Furthermore, loss of p27 expression was significantly associated with lymph node metastasis ($P = 0.009$). However, p27 down-regulation had no influence on overall survival using univariate analysis. **Conclusions.** The trend of reduced p27 expression in microinvasive and invasive carcinomas suggests that down-regulation of p27 expression is strongly linked to neoplastic transformation of cervical epithelium, and inactivation of p27 may be an early event in cervical carcinogenesis. Moreover, loss of p27 expression was related to lymph node metastasis in cervical carcinoma. These results imply that inactivation of p27 is associated with highly aggressive phenotype of cervical carcinoma. (c) 2002 Elsevier Science (USA).