EXPRESSION OF p^{53}, c-*erb*B-2, PCNA AND DAN CONTENT IN LUNG CARCINOMA

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The expression of p^{53} protein, c-*erb*B-2 oncoprotein, proliferating cell nuclear antigen (PCNA) were studied by the streptavidin peroxidase conjugated (S–P) immunohistochemical method and DNA content *in situ* was tested, in order to explore the significance of p^{53}, c-*erb*B-2, PCNA in primary lung carcinoma.

MATERIALS AND METHODS

Sixty-seven primary lung carcinoma specimen were resected in the Department of Surgery, Wuhan General Hospital of PLA. Tumors were classified histologically into 30 squamous cell carcinoma, 25 adenocarcinoma and 12 small cell carcinoma depending on the World Health Organization criteria (1981).

Three antibodies were used for immunohistochemistry, p^{53} and PCNA were detected by mouse monoclonal antibody. C-*erb*B-2 by a polyclonal antibody. Both antibodies were purchased from Fuzhou Maxin Biotech Co. All immunohistochemical staining was done on 5 μm sections using S–P. In p^{53} and PCNA staining of lung carcinoma, the positive substances were localized in the cell nuclei. The c-*erb*B-2 oncoprotein staining located predominantly at the cell membrane, but relatively rare at the cytoplasm, which was analyzed using semi-quantitative technique according to combining the number of positive cells with the intensity of staining reaction.

Feulgen's method was applied to DNA staining. The DNA content was measured by TOTY-400 image analysis system. All data were analyzed using x^2-test, ANOVA and spearman correlation analysis.

RESULTS

The expression of p^{53} protein, c-*erb*B-2 oncoprotein and PCNA in primary lung carcinoma was 40.29%, 38.81% and 85.07%, respectively. The p^{53} expression was associated with the smoking history of patients ($P<0.05$). There were no significant correlation between p^{53} expression and clinical pathology factors and prognosis ($P>0.05$). This study shows that expression of the c-*erb*B-2 oncoprotein was seen in squamous cell carcinoma and adenocarcinoma. None of the small cell lung carcinoma was positive for the c-*erb*B-2 oncoprotein.

Tumors from 14 (53.85%) of 26 cases with lymph node metastasis exhibited positive staining of c-*erb*B-2. By comparison, 12 (29.2%) of 41 cases without any lymph node metastasis exhibited positive staining of c-*erb*B-2 ($P<0.05$). The difference of the c-*erb*B-2 expression was highly significant among the survival ≤ 2y group, 2y~5y group and ≥ 5y group ($P<0.01$).

The positive grading of PCNA was closely and positively correlated with TNM stages of lung carcinoma ($r=0.48734$, $P<0.01$), whereas it was negatively correlated with the survival time after operation ($r = -0.42951$, $P<0.01$). Besides, it was positively correlated with the positive grading of c-*erb*B-2 expression ($r = 0.26218$, $P = 0.0321$).

The positive grading of PCNA was closely positively correlated with the DNA content of adenocarcinoma ($P<0.05$). The PCNA declination of positive grading was accompanied with the decrease in DNA content and the proportion of polyploid. Inversely, it was completely the very reverse. This relation was insignificant in the small cell lung carcinoma group.

DISCUSSION

There are no definite result in the relationship between expression of p^{53} protein, c-*erb*B-2 and histologic type, lymph node metastasis, TNM stage and prognosis of lung carcinoma in the literature. Our study showed that there was no significant correlation between p^{53} expression and the above prognostic factors of lung carcinoma. It was associated with smoking history in patient with lung carcinoma.

The results suggested that the p^{53} gene could be a common target of tobacco carcinogenesis in lung carcinoma. In addition, the expression of c-*erb*B-2 was associated with histologic type, lymph node metastasis and survival rate of lung carcinoma. Therefore, our results suggested that the expression of c-*erb*B-2 is one of the biologic markers to judge the histologic type and prognosis of lung carcinoma. The examination of PCNA and DNA content have been applied to study proliferation activity of tumor cell. But there are different viewpoints on evaluating its prognostic significance of lung carcinoma.

The results of our study proved that the positive grades of PCNA were positively correlated with the NDA contents and polyploid. While it was contrary to survival rate of lung carcinoma. The positive grading of PCNA increased with that of c-*erb*B-2. It indicated that the invasiveness of primary lung carcinoma is stronger when both of them expressed. Therefore, to detect the expression of PCNA and c-*erb*B-2 in tissue of lung carcinoma by immunohistochemical method is helpful for reflecting the proliferation activity of tumor cell and evaluating prognosis of lung carcinoma.

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