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Original Articles

Relationship between DNA ploidy, expression of ki-67 antigen and gastric cancer metastasis *

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Subject headings Ki-67 antigen; neoplasms metastasis; immunoc hemistry; DNA ploidy; stomach neoplasms/pathology

Abstract

AIM To evaluate the relationship between the expression of Ki-67 antigen and the pathobiological behaviours of gastric cancers especially their distant metastases.

METHODS Fifty-six specimens of gastric cancer routinely fixed in formalin and embedded in paraffin (FFEP) were studied by immunohistochemical method.

RESULTS Expression of Ki-67 antigen was significantly related to the distant metastases to liver, ovary and adrenal gland ($P<0.01$), but not related to the histological type, growth pattern, depth of invasion, histological differentiation and the metastases to local lymph nodes ($P>0.05$). Furthermore, the Ki-67 antigen expression was significantly related to the DNA aneuploidy pattern, which is closely related to poor prognosis ($P<0.05$).

CONCLUSION Overexpression of Ki-67 can be used as an objective marker of the proliferative activity for predicting prognosis of gastric cancer and metastatic potential to distant organs.

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INTRODUCTION

Ki-67 is a mouse monoclonal antibody which recognizes a nuclear antigen expressed in all phases of the cell cycle except Go and early G1[1]. And Ki-67 immunoreactivity can thus be used as biomarker for cell proliferation. Anothermethod to measure cell proliferation is flow cytometry. In our study, we detected 56 gastric cancer tissue specimens immunohistochemically by PcAb-Ki-67 (Dako, A047) and compared with DNA ploidy pattern in order to evaluate the relationship between the proliferative activity of gastric cancer cell and pathobiological behavior of gastric cancer, especially the relationship with the distant organ metastases.

MATERIALS AND METHODS

Materials

Fifty-six specimens of gastric cancer were collected from Cancer Institute of China Medical University. Among these 56 cases, no metastasis was found in 7 cases, 12 were accompanied with liver, 4 with ovarian, 1 with adrenal and 47 with lymph node metastasis. Tissue blocks from primary and metastatic tumours were chosen from each case.

Methods

PcAB to human Ki-67 antigen (A047) was used in this study to identify the proliferative activity of gastic cancer cell. The dilution for Ki-67 was 1:100. Sections were immunostained using the avidin-biotin-peroxidase complex method and pressure cooking was used to unmask Ki-67 antigen[2].

Evaluation of immunostaining

Four semi-quanti quantitative classes were used for grading: negative(-), no positive cells; weak positive (+), positive cells < 10%; moder ately positive (+ +), the positive cells between 10%-50%; strong positive (+ + +), the positive cells >50%.

DNA ploidy was measured by flow cytometry, the detailed procedures and the stand ard of evaluation followed the method reported previously[3].

RESULTS

Expression of the Ki-67 antigen was not related to WHO's classification and Lauren's classification ($P<0.05$). It was not related to the depth of local invasion of gastric cancer ($P>0.05$), growth pattern

($P > 0.05$) and local lymph nodes metastasis ($P > 0.05$). But the expression of Ki-67 was significantly related to the distant organ metastases ($P < 0.005$, Table 1) and also related to DNA aneuploidy pattern(Table 2).

Table 1 Relationship between expression of Ki-67 antigen and metast asis of gastric cancer

Metastasis (Mets)	*n*	Expression of Ki-67 antigen	
		+—+ +(%)	+ + +(%)
Non-Mets	7	3(42.9)	4(57.1)
LN Mets	32	23(71.9)	9(28.1)
Distant organ Mets	17	3(17.6)	14(82.4)[b]
Total	56	29(51.8)	27(48.2)

[b]$P<0.01$, *vs* LN (lymph node).

Table 2 Relationship between expression of Ki-67 antigen and DNA ploidy

DNA ploidy	*n*	Expression of Ki-67 antigen	
		+—+ +(%)	+ + +(%)
Di(Tetra)ploid	35	22(62.9)	13(37.1)
Aneuploid	21	7(33.3)	14(66.7)[a]

[a]$P<0.05$.

DISCUSSION

Proliferative activity of cancer cells was closely related to the biological behavior of carcinoma, especially the invasion, metastasis and prognosis. In this study, the results showed that Ki-67 could be used as a marker to measure the proliferative activity of gastric cancer cells and predict the potential of metastasis to distant organs of gastric cancer. The method was simple and quick. The detection of Ki-67 antigen could be used as a useful marker to foretell the high risk of the metastases to distant organs and predict the prognosis of gastric cancer.

DNA aneuploidy was one of the markers of malignant tumour cells. Xin, *et al* had reported that aneuploidy DNA pattern may be related to the development of distant organ metastases, especially through the blood vascular system[4]. The results of this study showed that DNA aneuploidy was related to the expression of Ki-67, the latter was also closely related to the distant met astases ($P < 0.01$). These suggested that the expression of Ki-67 and aneuploidy DNA pattern are two objective markers which may be valuable in predicting high potential of metastases to the distant organs, and the combined detecti on of these two markers could be a more useful method for predicting metastases to the distant organs and prognosis.

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