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Clinical significance of Fas antigen expression in gastric carcinoma *

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INTRODUCTION

In order to determine whether Fas antigen plays a role in the gastric carcinogenic sequence, an immunohistochemical study of Fas antigen expression in gastric carcinoma and its relation to clinical status, pathomorphological parameters and prognosis was carried out and reported below.

MATERIALS AND METHODS

Histological specimens

Fifty-nine cases of surgically resected gastric carcinomas (male 37, female 22; mean age 55.6 years) were selected from the files of the Department of Pathol ogy of our hospital. All blocks were fixed in 10% formalin and embedded in paraffin. Serial sections were cut from each block in 4μm, HE stained and confirmed pathologically. All patients underwent curative resection, and followed up for 2.7 to 52 months.

Immunohistochemical methods

Immunohistochemical staining for Fas antigen was performed using SP technique. S lides were deparaffinized and then were hydrated and detected with immunotist chencal kit according to the mannal of the mountecturer. The sections were then counterstained with hematoxylin. With each batch of test samples, a positive control consisting of a tissue section from liver was evaluated. A negative control was prepared for each sample using an irrelevant antibody of the same isotype as the primary antibody. The immunostaining of Fas antigen was visually classified into negative and positive groups.

Statistics

Correlations between Fas antigen expression and clinicopathologic parameters were examined using Chi-square test. Survival data was analyzed by a log-rank test. $P<0.05$ was considered to be statistically significant.

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RESULTS

Expression of Fas antigen in gastric carcinoma

Twenty-seven (45.8%) of the 50 gastric carcinomas showed immunoreactivity for Fas antigen in gastric carcinoma cells. The Fas antigen immunoreactivity appeared brown or dark brown, which was mainly located in the cytoplasm (Figure 1), a few specimens simultaneously expressed Fas antigen on the cell membrane of tumor cells. Some of the mature lymphocytes infiltrating in the stroma of gastric carcinoma had Fas antigen expression with a strong staining intensity.

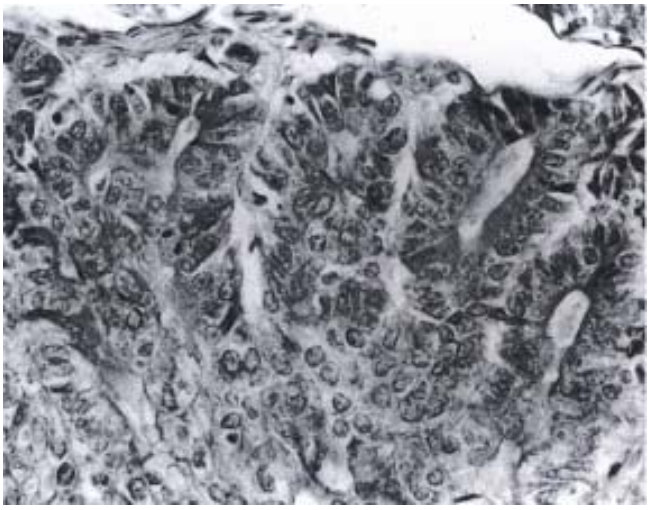

Figure 1 Immunoreactivity of Fas antigen detected in the cytoplasm of gastric carcinoma cells. SP×200

Correlation between Fas antigen expression and clinico-pathological parameters of gastric carcinomas

Fas antigen expression was related to clinical pathological staging of gastric carcinoma. The rate of Fas antigen expression was not correlated with patient age, sex, tumor size, grades of differentiation and depth of invasion ($P>0.05$). The immunoreactivity of Fas antigen was significantly associated with lymph node status and clinical stages of gastric carcinoma. Sixteen (61.5%) of 26 gastric carcinomas without lymph node metastasis were immunoreactive

versus 11 (33.3%) of 33 cases with lymph node metastasis ($P<0.05$). Twenty-one (58.3%) of 36 gastric carcinomas in clinical stages I and II were immunoreactive versus 6 (26.1%) of 23 gastric carcinomas in clinical stages III and IV ($P<0.05$).

Relationship between Fas antigen expression and prognosis

The survival rate of patients with Fas antigen expression was compared with that of those without Fas antigen expression. Patients with Fas antigen expression in gastric carcinomas showed a significantly longer survival period as compared with those without Fas antigen expression ($P<0.05$).

DISCUSSION

Fas antigen is a type I transmembrane protein, its molecular weight is 45 000, and it belongs to the tumor necrosis factor/ nerve growth factor receptor family[1]. Fas antigen as a receptor exists in the body and can induce a poptosis in target cells. In recent studies, Fas antigen expression has been ide ntified in various human organs, e. g. , heart, liver, lung, kidney, and ovary[2,3]. But, little is known about Fas antigen expression and its relationship with the biological behavior and prognosis of human gastric carcinoma.

In this study, we found that Fas antigen also expressed in gastric carcinoma tissues. Since Fas antigen is a transmembrane protein, it should appear both on the surface and in the cytoplasm of gastric carcinoma cells. But, in our study, most of the specimens expressed Fas antigen only in the cytoplasm of tumor cells, a few specimens expressed Fas antigen both on the surface and in the cytoplasm of tumor cells. There are several possible explanations for this. First, under pathological conditions, normal Fas antigen expression may be down-regulated, but expressi on of soluble Fas antigen is up regulated[4]. Second, Fas antigen may be affected by mutation on its DNA, or certain abnormalities may occur in the maturation process of this protein. Third, the structure of Fas antigen, which originally expressed on the surface, may be destroyed through a certain mechanism, e . g. , its binding site on the membrane undergoes proteolysis, and only cytoplasmic Fas antigen expression remains. However, the mechanism remains to be elucidated in future in vitro studies.

Our findings concerning the relationship between Fas antigen expression and the pathological characteristics of gastric carcinoma showed that Fas antigen expression could relate to lymph node status and clinical stages. The rate of Fas antigen expression was significantly higher in gastric carcinomas without lymph node metastasis than in those with lymph node metastasis, and in clinical stages I and II than in clinical stages III and IV gastric carcinomas. This indicated that aberrant Fas antigen expression may be involved in lymph node metastasis of gastric carcinoma. In addition, the survival period of patients with Fas antigen expression was longer than those without Fas antigen expression. The results demonstrated that Fas antigen expression may be of some value in predicting prognosis in patients with gastric carcinoma.

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