Expression of PTEN and KAI1 tumor suppressor genes in pancreatic carcinoma and its association with different pathological factors

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Abstract. Pancreatic carcinoma is a common cancer type with a poor prognosis. The aim of the present study was to examine the expression of tumor suppressor genes phosphatase and tensin homolog deleted in chromosome 10 (PTEN) and KAI1 in pancreatic carcinoma and its association with clinical pathological factors. A total of 50 hospitalized cases of pancreatic cancer including 28 males and 22 females aged 31-82 years were included in the present study. Ten cases of normal pancreatic tissue were obtained from cadavers and served as the controls. The pancreatic specimens were embedded in paraffin blocks and slides were prepared for immunohistochemical analysis to determine the expression of PTEN and KAI1 in normal pancreatic tissue and pancreatic carcinoma samples. The positive expression rate of PTEN in the normal pancreatic tissue was higher than that in pancreatic carcinoma (P<0.05), while the positive expression rate of KAI1 in the normal pancreatic tissue was lower than that in pancreatic carcinoma (P<0.05). Pathological factors such as clinical stage of disease, histological grade and the presence or absence of lymphatic metastasis significantly affected the expression of PTEN and KAI1 (P<0.05). In conclusion, the positive expression of PTEN and KAI1 in pancreatic carcinoma is closely associated with the development of pancreatic carcinoma.

Introduction

Pancreatic carcinoma is a common type of cancer that is difficult to detect at the early stage owing to its latency and which has a poor prognosis. A possible reason for this is that phosphatase activity of tumor suppressor gene phosphatase and tensin homolog deleted in chromosome 10 (PTEN) induces immoderate growth of genes (1,2). The PTEN protein is widely expressed throughout the body and acts as a phosphatase for inhibition of the AKT signaling pathway. It is also one of the most commonly lost tumor suppressors in cancer. Mutations or deletions in PTEN inactivate its enzymatic activity leading to increased cell proliferation and reduced cell death (3).

Tumor metastasis suppressor gene, KAI1, also known as CD82, has been reported to be associated with tumor metastasis and prognosis (4,5). KAI1 is a member of the tetraspanin family based on its structural basis and as a metastatic suppressor gene based on functional grounds. Loss of KAI1 expression is associated with advanced stages of various human malignancies and results in invasive and metastatic behavior of tumor cells.

In the present study, we investigated the expression of PTEN and KAI1 tumor suppressor genes by determining their protein expression in pancreatic carcinoma through immunohistochemistry (IHC) to evaluate the clinical significance of the proteins in pancreatic cancer progression.

Materials and methods

Clinical samples. Pancreatic carcinoma samples were obtained from 50 hospitalized cases in the Xiangyang Hospital between 2008 and 2012. There were 28 males and 22 females aged 31-82 years, with an average age of 53.8±11.4 years. The cases were classified according to the TNM stage (6), with 8 cases in stage I, 15 cases in stage II, 24 cases in stage III and 3 cases in stage IV. For those cases, histological grade and case number, and presence or absence of lymphatic metastasis and case number are shown in Table I. In addition, 10 cases of normal pancreatic tissue samples obtained from the cadavers of 6 men and 4 women, aged 33-79 years, served as the control. The clinical specimens were embedded in paraffin blocks for analysis.

IHC for PTEN and KAI1. The pancreatic carcinoma samples were sectioned into 4 µm slices prior to dewaxing and hydration. Subsequently, the sections were stained with diaminobenzidine and stained with hematoxylin. Phosphate-buffered saline was used as a negative control. The reaction was stopped
immediately after color was developed in the experimental samples. The primary antibodies used were rabbit anti-PTEN monoclonal antibody (1:100; OriGene Technologies, Inc., Rockville, MD, USA) and rabbit anti-KAI1/CD82 monoclonal antibody (1:100; OriGene Technologies, Inc.). For the secondary antibody, goat anti-rabbit antibody (1:100, BD Biosciences,}

Table I. PTEN expression in pancreatic carcinoma for three different pathological factors. a

A, Expression of PTEN by considering clinical stage (I-IV) of pancreatic cancer as pathological factor

| Clinical stages | No. | Positive expression, no. | Positive expression rate, % | P-value |
|-----------------|-----|--------------------------|-----------------------------|---------|
| I, II           | 23  | 14                       | 60.87                       | <0.05   |
| III, IV         | 27  | 5                        | 18.52                       | <0.05   |

B, Expression of PTEN by considering histological grade for cancerous pancreatic tissue as pathological factor

| Histological grade | No. | Positive expression, no. | Positive expression rate, % | P-value |
|--------------------|-----|--------------------------|-----------------------------|---------|
| High differentiation| 12  | 8                        | 66.67                       | <0.05   |
| Intermediate differentiation | 22  | 8                        | 36.37                       | <0.05   |
| Poor differentiation | 16  | 3                        | 18.75                       | <0.05   |

C, Expression of PTEN by considering lymphatic metastasis of pancreas as pathological factor

| Lymphatic metastasis | No. | Positive expression, no. | Positive expression rate, % | P-value |
|----------------------|-----|--------------------------|-----------------------------|---------|
| No                   | 21  | 12                       | 57.15                       | <0.05   |
| Yes                  | 29  | 7                        | 24.14                       | <0.05   |

aP<0.05 is considered as statistically significant. PTEN, phosphatase and tensin homolog deleted in chromosome 10.

Table II. KAI1 expression in pancreatic carcinoma for three different pathological factors. a

A, Expression of KAI1 by considering clinical stage (I-IV) of pancreatic cancer as pathological factor

| Clinical stages | No. | Positive expression, no. | Positive expression rate, % | P-value |
|-----------------|-----|--------------------------|-----------------------------|---------|
| I, II           | 23  | 11                       | 47.82                       | <0.05   |
| III, IV         | 27  | 22                       | 96.30                       | <0.05   |

B, Expression of KAI1 by considering histological grade of pancreatic cancer as pathological factor

| Histological grade | No. | Positive expression, no. | Positive expression rate, % | P-value |
|--------------------|-----|--------------------------|-----------------------------|---------|
| High differentiation| 16  | 15                       | 93.75                       | <0.05   |
| Intermediate differentiation | 22  | 15                       | 68.19                       | <0.05   |
| Poor differentiation | 12  | 5                        | 41.67                       | <0.05   |

C, Expression of KAI1 by considering lymphatic metastasis of pancreas as pathological factor

| Lymphatic metastasis | No. | Positive expression, no. | Positive expression rate, % | P-value |
|----------------------|-----|--------------------------|-----------------------------|---------|
| No                   | 21  | 10                       | 47.62                       | <0.05   |
| Yes                  | 29  | 28                       | 96.55                       | <0.05   |

aP<0.05 is considered as statistically significant. PTEN, phosphatase and tensin homolog deleted in chromosome 10.
Pancreatic cancer is characterized by an increasingly high incidence. The incidence of pancreatic cancer has been on the increase. Detection of pancreatic cancer poses a challenge in the presence or absence of lymphatic metastasis. The expression of KAI1 in lymphatic metastasis was significantly higher than that in the early pancreatic carcinoma (27,28). In the present study, we identified that the expression of KAI1 in clinically advanced pancreatic carcinoma was significantly higher than that in the clinically early pancreatic carcinoma. In addition, the expression of KAI1 in pancreatic carcinoma with high cell differentiation was significantly lower than that in pancreatic carcinoma with low cell differentiation.

In conclusion, clinical stages, histological grade, as well as presence or absence of lymphatic metastasis affect the positive expression of PTEN and KAI1 in pancreatic carcinoma. The two genes are closely associated with lymphatic metastasis and the degree of tumor malignancy.

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