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Clinical value of combined detection of serum APE1-Aabs and CEACAM-1 in the diagnosis of colorectal cancer

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Abstract. – OBJECTIVE: To analyze the clinical value of combined detection of serum APE1-Aabs and CEACAM-1 in pathological diagnosis of colorectal cancer.

PATIENTS AND METHODS: From December 2014 to July 2016, 60 patients with colorectal cancer and 50 healthy subjects were enrolled in this study. The levels of APE1-AAbs, CEACAM-1 and CEA in the serum were measured, and the clinical value of each index in the diagnosis of colorectal cancer was analyzed.

RESULTS: The level of serum APE1-AAbs in colorectal cancer group was significantly higher than that in healthy control group ($p < 0.05$). The levels of serum CEACAM-1 and CEA in colorectal cancer patients were significantly higher than those in healthy control group ($p < 0.05$). The sensitivity and accuracy of APE1-AAbs and CEACAM-1 in the diagnosis of colorectal cancer were significantly higher than separate detection of APE1-AAbs, CEACAM-1 or CEA.

CONCLUSIONS: Combined detection of serum APE1-AAbs and CEACAM-1 has the advantages of high sensitivity and good accuracy in the diagnosis of colorectal cancer, and it is worthy to be popularized in clinical practice.

Key Words:
APE1-Aabs, CEACAM-1, Colorectal cancer, Diagnosis.

Introduction

Colorectal cancer is a common disease in clinic, but there are still few tumor markers in the early diagnosis of colorectal cancer[1]. Therefore, the selection of appropriate biomarkers in the diagnosis and evaluation of colorectum has important clinical value[2]. The clinical study found that carcinoembryonic antigen related cell adhesion molecule 1 (CEACAM-1) is closely related to the development of tumor, since CEACAM-1 was in the peripheral blood of the human body, and was distributed by the blood to the tissues and organs. Therefore, it can be used as one of the important biomarkers for the diagnosis and evaluation of tumor patients[3]. Apurinic/Apyrimidinic Endonuclease 1 (APE1), also known as redox factor-1, is widely present in tissues and organs[4]. Some scholars have found that APE1 autoantibodies (APE1-AAbs) are also present in peripheral blood of cancer patients and can be used as one of the indicators to evaluate the condition of cancer patients. However, the combination of serum APE1-Aabs and CEACAM-1 in the evaluation of the clinical application of tumor patients is still rarely reported. In this study, 60 patients with colorectal cancer in our hospital from December 2014 to July 2016 were selected, and clinical value of combined detection of serum APE1-Aabs and CEACAM-1 in the diagnosis of colorectal cancer were evaluated.

Patients and Methods

Patients' Information

Patients with colorectal cancer treated in our hospital from December 2014 to July 2016 were selected, including 41 males and 19 females, age ranged from 25 to 91 (mean age: 62.83 ± 10.23): 24 cases of smoking history, 36 cases of no smoking history, 27 cases of drinking history, 33 cases of non-alcoholic history, 13 cases of family history of cancer, 47 cases of tumor-free family history. In the same period, 50 healthy patients were selected as the subjects, including 26 males and 24 females, age ranged from 23-86 (mean age: 59.83 ± 8.38): 15 cases of smoking history, 35 cas-

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es of non-smoking history, 18 cases of drinking history, 32 cases of history of drinking, 7 cases of family history of tumor, 43 of cases no cancer family history. There were no significant differences in gender, age, smoking history, history of drinking and history of cancer in colorectal cancer group and healthy control group (p>0.05). All patients involved in this study were informed and signed informed consent. The research process was not affected by related materials, equipment and pharmaceutical enterprises. The above cases were confirmed by the hospital Ethics Committee Approval.

Inclusion and Exclusion Criteria

All patients in this study were eligible for the following criteria: (1) patients with colorectal cancer were confirmed by pathology; (2) patients with tumor lesion metastases; (3) patients with clinical data integrity; (4) patients involved in this study were informed and signed informed consent. Exclusion criteria: (1) patients with severe infection; (2) patients with other severe trauma; (3) patients who had autoimmune diseases; (4) patients with other malignant tumors; (5) patients retreated from the study.

Methods

In this study, all subjects were collected with fasting venous blood 3 mL. The blood was centrifuged for 10 min (3000 r/min). The serum was collected and APE1-AAbs levels were measured by APE1-AAbs assay kit (Tianjin Huabote Biotechnology Co., Ltd., Tianjin, China). CEACAM-1 levels in serum were detected by CEACAM-1 ELISA Assay Kit (Shanghai Maiyer Biotechnology Co., Ltd., Shanghai, China). All procedures were performed according to the kit instructions. The level of CEA in serum was measured by Roche COBASE 601 automatic chemiluminescence instrument (Roche Pharmaceutical Ltd, Shanghai, China) and original matching reagent.

Statistical Analysis

In this study, SPSS 19.0 (IBM Corp., IBM SPSS Statistics for Windows, Armonk, NY, USA) was used to store and process the original data. The X^2 test was used to analyze the count data. The t-test was used to analyze the difference of the measured data. The diagnostic value of each index was evaluated according to the pathological examination. $p < 0.05$ meant the difference was statistically significant.

Results

APE1-AAbs Test Results of Patients

The results of this study showed that the level of APE1-AAbs in colorectal cancer group was significantly higher than that in healthy control group, and the difference was statistically significant ($p < 0.05$) (Table I).

CEACAM-1 and CEA Test Results

The levels of CEACAM-1 and CEA in colorectal cancer group were significantly higher than those in healthy control group ($p < 0.05$), and the results were statistically significant (Table II).

Diagnostic Efficacy of Each Index

The results of this study show that the sensitivity and accuracy of APE1-AAbs and CEACAM-1 in the diagnosis of colorectal cancer were significantly higher than separate detection of APE1-AAbs, CEACAM-1 or CEA alone (Table III and Figure 1).

Discussion

At present, in the diagnosis of tumors, although the traditional CEA serum markers have a certain diagnostic value in the diagnosis of colorectal cancer, are still lacking serum markers with high sensitivity and specificity[5-7]. Therefore, it is important to find new early serological markers for the diagnosis of colorectal cancer. Some scholars have pointed out that antibodies and proteins related to DNA repair in the diagnosis of cancer and prognosis evaluation have great potential. APE1 is an important protein in the process of DNA damage repair, and it is highly expressed in tumor tissues such as liver cancer, non-small cell lung cancer, ovarian cancer and osteosarcoma. It mainly showed the ectopic expression of cytoplasm and increased expression intensity, and it is highly correlated with patients with radiotherapy and chemotherapy resistance, poor prognosis, etc. Therefore, APE1 can be used as a marker

Table I. Results of APE1-AAbs test (ng/mL).

Groups	Cases	APE1-AAbs
Colorectal cancer group	60	2.68 ± 0.34
Healthy control group	50	1.83 ± 0.31
t		9.321
p		0.000

Table II. Results of CEACAM-1 and CEA examination of the subjects (ng/mL).

Groups	Cases	CEACAM-1	CEA
Colorectal cancer group	60	10.38 ± 2.39	7.84 ± 1.23
Healthy control group	50	4.01 ± 0.92	2.55 ± 0.98
t		19.023	16.988
p		0.000	0.000

Table III. Diagnostic efficacy of each index (%).

Index	Sensitivity	Specificity	Accuracy
APE1-AAbs	62.73	85.38	74.67
CEACAM-1	51.02	98.05	72.03
CEA	46.98	97.48	74.29
APE1-AAbs + CEACAM-1	82.19	82.38	83.29
APE1-AAbs + CEA	70.94	83.01	80.30

for the evaluation of tumor tissue and serological markers[8]. The results of this work show a high expression of serum CEACAM-1 and CEA levels in patients with colorectal cancer. APE1 abnormal high expression can stimulate the body to secrete APE1-AAbs. Therefore, it is theoretically possible to evaluate the occurrence and development of APE1-AAbs by assessing the level of tumor. Studies have shown that APE1 protein is present in peripheral blood of cancer patients and can stimulate the body to produce antibodies. With the proliferation, necrosis, and apoptosis of tumor cells, the high expression of APE1 in the cancerous tissue was released into the blood, and the immune system was activated to synthesize and secrete APE1-AAbs[9]. CEACAM-1, also known as CD66aa or C-CAM, BGP is an important transmembrane protein in the epithelial, bone marrow, and other cell membranes, and it is an important member of the CEA protein family[10]. CEACAM-1 has some biological functions that regulate cell-cell adhesion by regulating signal transduction. Also, CEACAM-1 can induce epithelial cell apoptosis, inhibit epithelial cell proliferation and tumor cell growth, stimulate B cell proliferation, delay monocyte apoptosis, inhibit T cells, natural killer cell activation and cytotoxicity, and can promote endothelial cell movement and tumor cell invasion. It has been found that CEACAM-1 is closely related to the clinical stage of gastrointestinal cancer. This research found that serum CEACAM-1 and CEA levels of colorectal cancer patients were significantly higher than the healthy control group[11]. The diagnostic sensitivity and accuracy of only use APE1-AAbs, CEACAM-1 or CEA in the diagnosis of colorectal cancer were significantly lower than combined detection of APE1-AAbs and CEACAM-1 or combined detection of APE1-AAbs and CEA. Further analysis showed that the combined detection of APE1-AAbs and CEACAM-1 in the diagnosis of colorectal cancer was superior to the combined detection of APE1-AAbs and CEA. The combined detection of APE1-AAbs and CEACAM-1

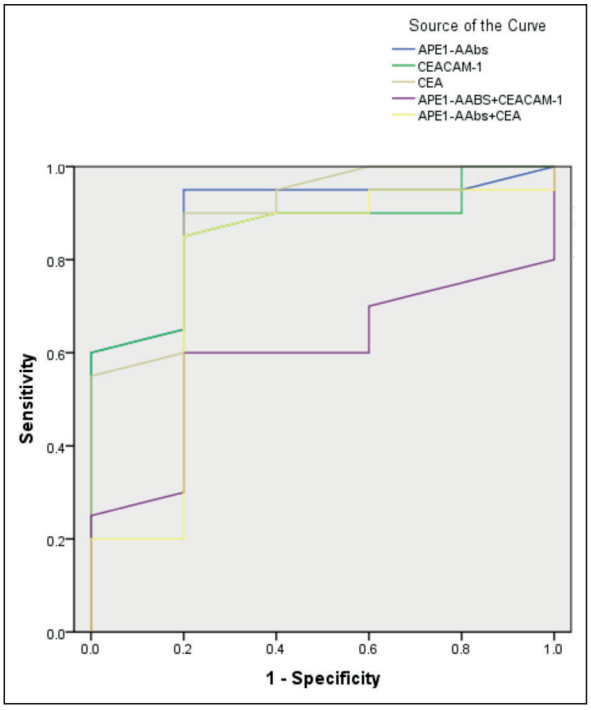

Figure 1. ROC curve.

in serum could effectively improve the diagnostic accuracy and sensitivity of colorectal cancer and has a certain diagnostic value. This could effectively improve the clinical detection rate of colorectal cancer in patients.

Conclusions

The combined detection of serum APE1-AAbs and CEACAM-1 had high sensitivity and good accuracy in the diagnosis of colorectal cancer. However, this study found that the two indicators of joint detection of the phenomenon of specific reduction, to be followed by the expansion of clinical samples in-depth study. However, the results of this work showed that the combination of two indicators may reduce the specificity, but we need to expand the number of clinical samples in future studies.

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Conflict of Interest
The Authors declare that they have no conflict of interests.

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