RESEARCH ARTICLE

Expression and Significance of TSGF, CEA and AFP in Patients Before and after Radical Surgery for Colon Cancer

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Abstract

Objective: To explore the expression and significance of tumor specific growth factor (TSGF), carcinoembryonic antigen (CEA) and alpha fetoprotein (AFP) in cancer tissue and serum of patients with colon cancer. Materials and Methods: Radical surgery for colon cancer was performed on 43 patients with laparoscopu under conditions of general anesthesia. The Elisa method was used to detect the levels of serum TSGF, CEA and AFP before and after radical operation, and cancer tissue underwent TSGF, CEA and AFP immunohistochemistry staining after laparoscopic surgery. The decreased conditions of serum TSGF, CEA and AFP in patients with colon cancer at different levels of differentiation and clinical stagings were analyzed, and the relationships of expression rates between histological types, colon cancer morphology, lymph node metastasis and TSGF, CEA as well as AFP in cancer tissue were assessed. Results: Compared with before radical surgery, the levels of serum TSGF, CEA and AFP decreased notably in patients after operations ($p<0.01$). The decreased degree of TSGF and CEA was the largest in patients with poorly differentiated cancer tissue ($p<0.01$), while that of AFP was noted in patients with moderately differentiated cancer tissue ($p<0.01$). The decreased degree of TSGF and AFP was the largest in patients at phase Dukes A ($p<0.01$), while that of CEA in patients at phase Dukes C ($p<0.01$). There were no significant differences among the positive expression rates of TSGF, CEA and AFP with different histological types and colon cancer morphologies ($p>0.05$). The positive expression rates of TSGF and CEA in patients with lymph node metastasis were significantly higher than those without lymph node metastasis ($p<0.01$). Conclusions: TSGF, CEA and AFP can be used to evaluate the effect of radical operation for colon cancer, and the changed levels of different markers are associated with tumor differentiation, clinical stating and presence or absence of lymph node metastasis.

Keywords: Colon cancer - tumor markers - clinical staging - immunohistochemistry - serum - TSGF - CEA - AFP

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Introduction

Colon cancer is a commonly-encountered malignant tumor in alimentary canal. With the improvement of current living standards and environmental degradation, its morbidity has been on the rise year by year (Akagi et al., 2013). Tumorigenesis is usually accompanied by a serious of abnormal genetic expression in the body, such as autoantibody and tumor markers, Similarly, the detection of these molecular levels are also applicable to tumor diagnosis and prognostic prediction (Molinari et al., 2013; Sasahira et al., 2013; Zhang et al., 2011). In the study, the expression and significance of tumor specific growth factor (TSGF), carcinoembryonic antigen (CEA) and alpha fetoprotein (AFP) in cancer tissue and serum of patients with colon cancer are investigated.

Materials and Methods

General data

Forty-three patients performed on radical operation for colon cancer in our hospital from Feb., 2009 to Apr., 2012 were selected, in which males were 26 cases, females 17 cases. They were 25-72 years old, and the mean age was (47.5±5.1) years old. The general data was as follows (Table 1).

Surgical Methods

Radical operation for colon cancer was performed on 43 patients with laparoscope under the condition of general anesthesia. According to different canceration sites, the corresponding positions were selected. For example, a head-low and foot-high rightward position was applicable

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to descending colon cancer, while a lithotomy position to sigmoid colon cancer (head-low and foot-high) and transverse colon cancer (head-high and foot-low). Carbon dioxide pneumoperitoneum was established, and three-hole technique was adopted to probe the viscera and tumor. The corresponding operations were performed based on different sites. After the surgery, it should be paid attention to protecting the incision and suturing layer-by-layer to avoid the occurrence of dead space and incisional hernia.

Tumor markers

One month before and after radical operation, cubital venous blood from fasting patients was drawn in the morning, and its serum was separated after centrifugation and preserved at -20°C. Elisa method was used to detect the levels of serum TSGF, CEA and AFP, and cancer tissue was given TSGF, CEA and AFP immunohistochemistry staining after laparoscopic surgery. The positive cell count of TSGF, CEA and AFP taking up the tumor cell count < 10% was the negative, while > 10% was the positive. The decreased conditions of serum TSGF, CEA and AFP in patients with colon cancer at different levels of differentiation and clinical stagings were analyzed, and the relationships of expression rates between histological types, colon cancer morphology, lymph node metastasis and TSGF, CEA as well as AFP in cancer tissue were observed.

Statistical data analysis

SPSS10.0 statistical software was applied to conduct a statistical analysis. t test was used to compare the means in two groups, and measurement data was expressed by (mean ± standard deviation). $p<0.05$ was represented differences had statistical significance.

Table 1. General Data of Patients Performed on Radical Operation for Colon Cancer (n=43)

Classifications	Number of cases	%
Cancer tissue types		
High differentiation	20	46.5
Moderate differentiation	13	30.2
Poor differentiation	10	23.3
Clinical staging		
Phase Dukes A	17	39.5
Phase Dukes B	14	32.6
Phase Dukes C	12	27.9
Pathogenic sites		
Sigmoid colon	23	53.5
Ascending colon	12	27.9
Descending colon	8	18.6

Results

Levels of serum TSGF, CEA and AFP before and after radical operation

Compared with radical operation before, the levels of serum TSGF, CEA and AFP decreased notably in patients after radical operation, and significant difference was presented ($p<0.01$) (Table 2).

Decreased conditions of serum TSGF, CEA and AFP at different levels of differentiation and clinical stagings

The differential levels of serum TSGF, CEA and AFP in patients with colon cancer before and after radical operation were calculated in the study. The decreased conditions of serum TSGF, CEA and AFP at different levels of differentiation and clinical stagings were different in patients with colon cancer before and after radical operation. The decreased degree of TSGF and CEA was the largest in patients with poorly differentiated cancer tissue ($p<0.01$), while that of AFP in patients with moderately differentiated cancer tissue ($p<0.01$). The decreased degree of TSGF and AFP was the largest in patients at phase Dukes A ($p<0.01$), while that of CEA in patients at phase Dukes C ($p<0.01$) (Table 3).

Results of TSGF, CEA and AFP immunohistochemistry staining in patients with colon cancer

The positive staining of TSGF and CEA was expressed in cytoplasm, while that of AFP in nucleuses or cytoplasm. The positive expression rates of TSGF, CEA and AFP in tumor tissue of patients with colon cancer were 65.11% (28/43), 69.77% (30/43) and 11.63% (5/43), respectively. It could be seen in tables 4 and 5, there were no significant

Table 2. Comparison on the Levels of Serum TSGF, CEA and AFP Before and after Radical Operation (n=43, $\overline{\chi}\pm s$)

Items	Before radical operation	After radical operation
TSGF/U·mL^{-1}	77.33±7.02	72.14±6.93**
CEA/ng·mL^{-1}	17.91±2.34	9.75±0.93**
AFP/ ng·mL^{-1}	35.14±3.78	28.44±2.94**

Compared with radical operation before, **$p<0.01$

Table 3. Comparison on the Levels of Serum TSGF, CEA and AFP at Different Levels of Differentiation and Clinical Stagings ($\overline{\chi}\pm s$)

Items	Number of cases	TSGF/U·mL^{-1}	CEA/ng·mL^{-1}	AFP/ ng·mL^{-1}
Differentiation degrees				
Poor differentiation	10	5.54±0.51	9.46±0.86	15.04±1.66
Moderate differentiation	13	4.75±0.43**	6.92±0.71**	18.79±1.77**
High differentiation	20	3.46±0.36**$^{\#\#}$	4.85±0.46**$^{\#\#}$	9.67±1.07**$^{\#\#}$
Clinical stagings				
Phase Dukes A	17	5.14±0.56	6.57±0.79	17.34±1.65
Phase Dukes B	14	2.99±0.34$^{\triangle\triangle}$	6.04±0.86	13.56±1.45$^{\triangle\triangle}$
Phase Dukes C	12	1.56±0.21$^{\triangle\triangle\blacktriangle\blacktriangle}$	11.03±1.24$^{\triangle\triangle\blacktriangle\blacktriangle}$	10.07±1.43$^{\triangle\triangle\blacktriangle\blacktriangle}$

Compared with poorly differentiated patients, **$p<0.01$; Compared with moderately differentiated patients, $^{\#\#}p<0.01$. Compared with the patients at phase Dukes A, $^{\triangle\triangle}p<0.01$; Compared with the patients at phase Dukes B, $^{\blacktriangle\blacktriangle}p<0.01$

Table 4. Expression of Different Histological Types of TSGF, CEA and AFP [n(%)]

Histological Types	Number of cases	TSGF	CEA	AFP
Papillary adenocarcinoma	22	16(72.72)	17(77.27)	2(9.09)
Tubular adenocarcinoma	10	6(60.00)	7(70.00)	1(10.00)
mucous adenocarcinoma	9	5(55.56)	5(55.56)	2(22.22)
Signet-ring cell carcinoma	2	1(50.00)	1(50.00)	0(00.00)

Table 5. Relationships Between TSGF, CEA, AFP and Different Morphologies of Colon Cancer as Well as Lymph Node Metastasis [n(%)]

Histological Types	Number of cases	TSGF	CEA	AFP
Colon cancer morphology				
Nodular carcinoma	20	14(70.00)	14(70.00)	2(10.00)
Annular carcinoma	10	6(60.00)	7(70.00)	2(5.00)
Ulcerative carcinoma	13	8(61.54)	9(69.23)	1(7.69)
Lymph node metastasis				
Metastasis	30	24(80.00)**	27(90.00)**	3(10.00)
Non-metastasis	13	4(30.77)	3(23.08)	2(15.38)

Compared with the patients without lymph node metastasis, $^{**}p<0.01$

differences among the positive expressions of TSGF, CEA and AFP with different histological types and colon cancer morphologies ($p>0.05$); the positive expression rates of TSGF and CEA in patients with lymph node metastasis were significantly higher than those without lymph node metastasis ($p<0.01$).

Discussion

Tumor markers are widely applied to evaluate tumor diagnosis, treatment and prognosis. Relevant studies revealed that the levels of tumor markers can be changed before and after treatment, whereas its specific mechanism still remains undefined. Meanwhile, some studies demonstrated that it may be related to decreased tumor burden (Church et al., 2012; Clark et al., 2012; Wu et al., 2013). Colon cancer, a sort of malignant tumor in alimentary canal, has higher incidence and mortality. Hence, how to assess its therapeutic effect becomes an important problem in medical field (de Cuba et al., 2012; Benhaim et al., 2012; Yu, et al., 2012). In the study, three representative tumor markers TSGF, CEA and AFP are screened to explore their level variations before and after radical operation for colon cancer as well as the decreased levels at different clinical stagings and differentiation degrees, which are of great theoretical and clinical research value.

CEA, an acid glycoprotein, contains human CEA determinant. Its level in fetal alimentary canal will be reduced after birth, whereas as one of nonspecific tumor markers, its level can be elevated in the patients with malignant tumors such as breast cancer, gastrointestinal cancer, thyroid cancer and lung cancer (Turriziani et al., 2012; Spelt et al., 2012). Due to poor sensitivity, its therapeutic effect of single application is not significant, so it is frequently used in combination with other tumor markers. Elevated CEA demonstrated that the metastasis occurred in tumor or the tumor is at an advanced stage (Stillwell et al., 2011). In 1976, the study made by Herrer, et al. had revealed the staging effect of CEA on colon cancer, namely preoperative elevated CEA level suggests the tumor is at an advanced stage (Herrere et al., 1979). Later, a lot of researchers also believed that preoperative CEA level was associated with the tumor range (Yamashita et al., 2009; Fiorentino et al., 2010; Xu et al., 2011). When CEA level > 20 ng/mL, the patients at phase Ducks D accounted for 37%. Some early studies also confirmed CEA level was related to distant metastasis of primary tumor, regional lymph nodes and infiltration depth (Lupinacci et al., 2007; Søreide et al., 2009). The initial tumor size at phases A and B was related to CEA level, suggesting that as an independent prognostic index, CEA level is directly proportional to the enlargement of tumor volume (Zorcolo, 2006; Duffy et al., 2007). The increase of CEA level implies high recurrence rate and worse rehabilitation as well as prognosis. As the most important staging factor, the occurrence of pathological stating reveals elevated CEA can decrease the survival rate of patients. In adults, the increase of AFP can occur in serum in about 80% of patients with liver cancer, and its positive rate is 50% in generative cell tumors. Meanwhile, its increase can also occur in patients with other gastrointestinal tubal tumors by varying degrees like pancreatic cancer, lung cancer and liver cirrhosis (Ławicki et al., 2002; Amayo et al., 2009). Elevated AFP level is very common in patients with colon cancer, but its expression is almost absent in tumor tissue.

TSGF, a special substance discovered by Canadian scientists, is produced by malignant tumor cells (Koukourakis et al., 2011; Efferth, 2012; Duffy, 2013). As a new tumor marker, it can promote tumor formation and growth as well as proliferation of a large amount of peripheral capillaries. Positive TSGF can be detected out among dozens of malignant tumors, including different pathological types of squamous carcinoma, adenocarcinoma, hematologic tumor and glioma, confirming that TSGF is a common substance of malignant tumors, with a dual function of tumor types and spectrum (Yu et al., 2009; Pritchard et al., 2011). TSGF level can immediately increase significantly at an early stage of tumors, hence, it can be used to detect early tumors (Zhou et al., 2012). A lot of studies have confirmed that TSGF has better specificity and sensitivity in diagnosis of early malignant tumors.

The results in the study demonstrated that the levels of three markers obviously decreased one month after operation, suggesting that radical operation for colon cancer can effectively alleviate the tumor burden in patients. The influences of tumor clinical staging and differentiation on decreased marker levels were also analyzed, it was found that the largest decreased level of three markers were different. For example, AFP occurred at phase Dukes A and moderately differentiated cancer tissue, CEA at phase Dukes C and poorly differentiated cancer tissue, and TSGF at phase Dukes A and poorly differentiated cancer tissue, illustrating that different parameters can affect the decreased level of tumor markers. In addition, the results in the study also showed that there were no significant differences among the positive expressions of TSGF, CEA and AFP with different histological types and colon cancer morphologies; the positive expression rates of TSGF and CEA in patients

with lymph node metastasis were significantly higher than those without lymph node metastasis. Thus it can be seen that TSGF, CEA and AFP can be used to evaluate the effect of radical operation for colon cancer, and tumor differentiation, clinical staging and presence or absence of lymph node metastasis can affect the changed levels of different markers.

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