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Value of serum VEGFC content detection for evaluating the clinical pathological characteristics and malignant degree of esophageal cancer

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ABSTRACT

Objective: To analyze serum VEGF-C content in patients with esophageal cancer and its correlation with tumor stage, lymph node metastasis and cancer cell viability. **Methods:** A total of 112 patients with esophageal cancer treated in our hospital were selected as observation group, healthy subjects receiving physical examination in our hospital during the same time were selected as control group, serum VEGF-C content was compared between two groups of patients, and the correlation between VEGF-C level and tumor stage, lymph node metastasis as well as cancer cell viability was analyzed. **Results:** Serum VEGF-C level of observation group was higher than that of normal control group; serum tumor markers SCC, CEA, CA199, CA125 and CA50 levels were higher than those of normal control group; serum VEGF-C level of patients with esophageal cancer was positively correlated with tumor stage, lymph node metastasis and cancer cell viability. **Conclusion:** Serum VEGF-C content in patients with esophageal cancer is well correlated with tumor stage, lymph node metastasis and cancer cell viability, and regular detection of VEGF-C level can be the effective means to evaluate the therapeutic effect and predict treatment outcome.

1. Introduction

Esophageal cancer is one of the most common malignant digestive system tumors, it is without obvious early symptoms and characterized by jumpy disease progression, the current treatment effect is not ideal, and choosing appropriate monitoring indicators is quite important for accurately assessing the disease, judging therapeutic effect and predicting long-term results[1,2]. Vascular endothelial growth factor-C (VEGF-C) is a specific factor that promotes lymphangion generation, participates in tumor lymphangion generation and regional lymph node metastasis, and is an important factor in malignancy increase and lymphatic metastasis of tumor[3,4]. Clinical study has shown that most esophageal cancer patients with lymphatic metastasis are with high expression of VEGF-C, and early detection of VEGF-C level is expected to accurately judge the condition of esophageal cancer and take proper treatment measures[5]. In the study, serum VEGF-C content in patients with esophageal cancer and its correlation with tumor stage, lymph node metastasis and cancer cell viability were mainly analyzed, now reported as follows:

2. Information and methods

2.1 Case selection

A total of 112 patients diagnosed with esophageal cancer in our hospital between April 2013 and March 2016 were selected as observation group, they were diagnosed by clinical pathology and never treated with radiotherapy and chemotherapy as well as targeted therapy, they were without severe liver and kidney dysfunction as well as autoimmune diseases, and they included 59 male cases and 53 female cases that were 45-72 years old and 61 years old in average; 98 healthy volunteers receiving physical examination in our hospital during the same period were selected

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as control group, and they included 50 male cases and 48 female cases that were 47-70 years old and 63 years old in average. This study obtained informed consent from the included subjects and the approval from the hospital ethics committee. Two groups of research subjects were not statistically different in basic information such as age and gender (P>0.05).

2.2 VEGF-C content detection

3 mL of fasting cubital venous blood was extracted from 112 patients with esophageal cancer and 98 healthy subjects and centrifuged at 4 000 r/min for 10 min, and then the supernatant was collected and placed in a -20 ℃ refrigerator for test. Enzyme-linked immunosorbent assay (ELISA) was used to determine serum vascular endothelial growth factor C (VEGF-C) levels of the included subjects, and the specific steps were in strict accordance with the kit instructions.

2.3 Cancer cell viability level detection

3 mL of fasting cubital venous blood was extracted from 112 patients with esophageal cancer and centrifuged to get supernatant, and then the enzyme-linked immunosorbent assay chemiluminescence (ELISA-CL) was used to determine tumor marker levels, including squamous cell carcinoma antigen (SCC), carcinoembryonic antigen (CEA), carbohydrate antigen 199 (CA199), carbohydrate antigen 125 (CA125) and carbohydrate antigen 50 (CA50).

2.4 Statistical methods

SPSS 21.0 software was used to statistically analyze the above data, measurement data between two groups was by t test, correlation analysis was by Pearson test and P<0.05 meant statistical significance in the obtained results.

3. Results

3.1 Serum VEGF-C levels

Comparison of serum VEGF-C levels between the two groups was as follows: the mean serum VEGF-C level of observation group was (318.72±25.93) pg/mL and the mean serum VEGF-C level of control group was (43.64±2.49) pg/mL. differences in serum VEGF-C levels were statistically significant between observation group and control group (P<0.05).

3.2 Relationship between serum VEGF-C level and tumor stage as well as lymph node metastasis

Analysis of serum VEGF-C levels between esophageal cancer patients with different tumor stages and lymph node metastasis was as follows: serum VEGF-C level in patients with TNM Ⅰ/Ⅱ stage was significantly lower than that in patients with TNM Ⅲ/Ⅳ stage, and serum VEGF-C level in patients without lymph node metastasis was lower than that in patients with lymph node metastasis (P<0.05), shown in Table 1.

Table 1.

Relationship between serum VEGF-C level and tumor stage as well as lymph node metastasis.

Clinical pathological features	Groups	n	VEGF-C (pg/mL)
TNM stage	Ⅰ/Ⅱ stage	65	209.71±17.62
	Ⅲ/Ⅳ stage	47	472.43±35.75
	T		8.253
	P		＜0.05
Lymph node metastasis	Without	69	231.24±14.89
	With	43	463.55±30.61
	T		7.931
	P		＜0.05

3.3 Serum tumor markers

Analysis of serum tumor markers SCC, CEA, CA199, CA125 and CA50 between two groups of subjects was as follows: serum SCC, CEA, CA199, CA125 and CA50 levels of observation group were significantly higher than those of normal control group. Differences in serum SCC, CEA, CA199, CA125 and CA50 levels were statistically significant between two groups of subjects (P<0.05), shown in Table 2.

3.4 Correlation between serum VEGF-C level and cancer cell viability

Table 2.

Comparison of serum tumor marker levels between two groups of subjects.

Groups	n	SCC (ng/mL)	CEA (ng/mL)	CA199 (U/mL)	CA125 (U/mL)	CA50 (U/mL)
Observation	112	5.72±0.56	149.82±13.74	209.83±12.07	172.73±12.28	38.91±2.44
Control	98	1.13±0.11	4.81±0.68	33.62±3.87	25.62±2.33	4.02±0.36
t		6.383	7.282	9.834	8.637	8.232
P		＜0.05	＜0.05	＜0.05	＜0.05	＜0.05

Pearson analysis of the correlation between serum VEGF-C level and tumor marker levels in patients with esophageal cancer was shown in Table 3: serum VEGF-C level in patients with esophageal cancer was positively correlated with tumor markers SCC, CEA, CA199, CA125 and CA50 levels, and the determination coefficients r^2 were 0.521, 0.497, 0.561, 0.558 and 0.572 respectively.

Table 3.

Correlation between serum VEGF-C level and cancer cell viability.

Parameter	Regression coefficient b	Determination coefficient r^2	*T* value	*P* value
SCC	2.763	0.521	6.67	0.025
CEA	2.662	0.497	7.32	0.016
CA199	2.592	0.561	6.97	0.018
CA125	2.671	0.558	6.86	0.021
CA50	2.895	0.572	7.63	0.014

4. Discussion

The action of various cytokines in tumor microenvironment is the key link of cancer infiltration and metastasis, vascular endothelial growth factor (VEGF) is the research focus and hot spot in recent years, studies have shown that VEGF is highly expressed in many malignant tumor tissues, and it is the necessary factor for tumor progression, recurrence and metastasis[6,7]. VEGF-C, also known as the lymphatic growth factor, is a newly discovered member of the VEGF family, it was first cloned and isolated from prostate cancer strains, and it can be combined with VEGFR-3 and then adjust tumor angiogenesis as well as promote tumor cells to enter into lymph vessels and spread through the lymphatic system. Studies have found that VEGF-C is closely related to gastric cancer, thyroid cancer, prostate cancer and other tumor progression, and given the high incidence of esophageal cancer, the relationship between VEGF-C and esophageal cancer has received high clinical attention[8,9].

Sun ZG[10] detects the VEGF-C gene expression in esophageal cancer cell lines and then finds that there is VEGF-C mRNA expression in more than 80% of the esophageal cancer cell lines. Mao Guang-xian[11] has detected VEGF-C staining in cytoplasm of squamous epithelial cells of highly atypical hyperplasia and carcinoma in situ, indicating that VEGF-C is highly connected to the incidence of esophageal cancer. In the study, serum VEGF-C levels in patients with esophageal cancer and normal subjects were detected at first, and the results showed that the mean serum VEGF-C content of patients with esophageal cancer was higher, which is closely related to the vascular invasion and lymphatic metastasis in tumor cells, and indicates that VEGF-C occupies an important position in the occurrence and development of esophageal cancer. VEGF-C/VEGFR-3 signal system can promote lymphangiogenesis, it was also involved in the occurrence and development of esophageal cancer, but its different expression in esophageal cancer patients with different stages and lymph node metastasis needs further analysis to understand. Patients with esophageal cancer were further grouped according to TNM staging and lymph node metastasis, serum VEGF levels in esophageal cancer patients with different stages and grades were further analyzed, and the results showed that the serum VEGF-C level was lower in esophageal cancer patients with TNM Ⅰ/Ⅱ stage and without lymph node metastasis, indicating that the serum VEGF-C level is directly related to esophageal cancer stages and lymph node metastasis or not, and high levels of VEGF-C is directly involved in tumor progression and metastasis.

Tumor markers are the chemical substances that reflect tumor existence, and their application value in the digestive system tumors is far more than in tumors of other parts. Squamous cell carcinoma antigen (SCC) is a highly specific tumor marker for squamous cancer, its concentration increases along with the disease aggravation, and it can be used to detect tumor recurrence and metastasis, evaluate prognosis and so on[12,13]. Carcinoembryonic antigen (CEA) belongs to the protein polysaccharide conjugate, widely exists in the entoderm-derived digestive system cancer, can also be slightly expressed in normal human serum, belongs to broad-spectrum tumor marker, is without high specificity and sensitivity, and is mostly used in the detection of tumor recurrence[7]. Carbohydrate antigen 199 (CA199) is a mucin type of glycoprotein tumor marker, it is the gastrointestinal tract tumor-associated antigen in the blood circulation, its joint detection with CEA can improve the sensitivity, and when the treatment is effective, CA199 falls faster than the CEA. Carbohydrate antigen 125 (CA125) is derived from the coelomic epithelium of embryonic development period, it is the most sensitive tumor marker for ovarian cancer, and it is also discovered to be abnormally expressed in esophageal cancer at present[14,15]. Carbohydrate antigen 50 (CA50) is a kind of sialic acid ester and sialic acid glycoprotein, it is not usually expressed in normal tissue, its levels can rise sharply in the case of malignant transformation of tissue cells, it is highly sensitive, and it is a nonspecific broad-spectrum tumor marker. In the study, serum tumor marker levels were compared between patients with esophageal cancer and normal control group, and the results showed that the mean serum SCC, CEA, CA199, CA125 and CA50 levels of patients with esophageal cancer were higher, indicating that the proliferation activity of cancer cells is much higher than that of normal tissue cells.

SCC, CEA, CA199, CA125 and CA50 levels can directly reflect malignant tumor cell viability, the correlation between the VEGF-C level and the tumor marker values was analyzed at last in the study, and the results showed that serum VEGF-C level in patients with esophageal cancer was positively correlated with serum SCC, CEA, CA199, CA125 and CA50 values, indicating that VEGF-C level can also directly reflect tumor cell viability[8]. So the VEGF-C level can sensitively reflect the tumor stage, lymph node metastasis and

cancer cell viability in patients with esophageal cancer, it can play an important role in early diagnosis of esophageal cancer, judgment of treatment effect, evaluation of long-term prognosis and other aspects, and as serum VEGF-C level detection is easy to operate, at low cost and convenient for repeated measurement, it has brought convenience for clinical specific operations and patients themselves. To sum up, it is concluded as follows: serum VEGF-C content in patients with esophageal cancer is well correlated with tumor stage, lymph node metastasis and cancer cell viability, regular detection of VEGF-C level can be the effective means to evaluate the therapeutic effect and predict treatment outcome, and it's worth popularization and application in clinical practice in the future.

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