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Effects of combined treatment of bronchial arterial chemoembolization and radioactive particle implantation on tumor markers and T lymphocyte subsets in locally advanced non−small cell lung cancer

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ABSTRACT

Objective: To investigate the effects of bronchial arterial chemoembolization combined with radioactive particle implantation on the level of serum tumor markers and T lymphocyte subsets in patients with locally advanced non-small cell lung cancer. **Methods:** A total of 91 cases of locally advanced non-small cell lung cancer patients according to the random data table were divided into the control group (n=45) and observation group (n=46) according to the random data table. Patients in the control group was treated with bronchial arterial chemoembolization, on the basis of the control group, patients in the observation group were treated with radioactive particle implantation, the serum tumor markers and T lymphocyte subsets of the two groups were compared before and after treatment. **Results:** The levels of CEA, NSE, CA125, $CD4^+$, $CD8^+$, $CD4^+/CD8^+$ and NK in the two groups before the treatment were not statistically significant. Compared with the group before treatment, levels of CEA, NSE, CA125and $CD8^+$ of the two groups after treatment were significantly decreased, and after treatment the level of CEA, NSE, CA125and $CD8^+$ in the observation group was significantly lower than those of the control group; The levels of $CD4^+$, $CD4^+/CD8^+$ and NK in the two groups after treatment were significantly higher than those in the group before treatment, and the observation group levels were significantly higher than those of the control group. **Conclusion:** Bronchial artery embolization combined with radioactive particle implantation for locally advanced non-small cell lung cancer, can effectively reduce the serum tumor markers level, improve the level of T cell subsets of patients, has important clinical value.

1. Introduction

Lung cancer is one of the world's most common malignant tumor, its incidence and mortality rates are among the first tumor, including non-small cell lung cancer accounted for about 4/5 of lung cancer, because lung cancer symptoms are hidden,once diagnosed, mostly in the middle late stages, has lost the best time for surgical treatment[1]. Concurrent chemotherapy is an internationally accepted standard treatment, and has become the main means of clinical treatment, but its clinical effect is limited, toxic side effects are large[2,3]. Bronchial arterial chemoembolization and radioactive particle implantation are all new interventional therapy, and the treatment on lung cancer are better[4,5]. and T cell subsets in patients with locally advanced non-small cell lung cancer. The purpose of this study was to investigate the effects of combined treatment of bronchial arterial chemoembolization and radioactive seed implantation on serum tumor markers and T lymphocyte subsets in patients with locally advanced non-small cell lung cancer.

2. Research materials and methods

2.1. Research subjects

A total of 91 patients with locally advanced non-small cell lung cancer (NSCLC) who were enrolled in our hospital from January 2012 to January 2017 were selected as subjects. All patients were

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selected according to the screening criteria of this study. They were divided into control group (n=45) and observation group (n=46) according to the random data table method. 30 cases of male patients in the control group, 15 cases of female, aged 41 to 76 years, pathological types are divided into: adenocarcinoma in 22 cases, 19 cases of squamous cell carcinoma, squamous gland mixed in 4 cases; observation group, male 33 cases, female 13 Cases, aged 42 to 76 years, pathological types include: adenocarcinoma in 25 cases, 18 cases of squamous cell carcinoma, squamous gland mixed in 3 cases. The gender, age and pathological type of the two groups were similar, and the difference was not significant (P>0.05). The contents of this study are in accordance with the relevant standards of the Hospital Ethics Committee and are approved.

2.2. Screening criteria

Inclusion criteria: (1) all patients diagnosed by histology and pathology, are in line with local advanced non-small cell lung cancer-related diagnostic criteria[6]; (2) pathological stage ⅢA or ⅢB period; (3) all subjects complete data; (4) patients and their families are Informed consent, signed informed consent, and voluntarily joined the treatment.

Exclusion criteria: (1) patients with severe cardiopulmonary dysfunction, acute and chronic infectious diseases and autoimmune diseases; (2) one month before treatment to receive chemotherapy and immunotherapy; (3) contraindications to the study drug; (4) failed to follow the course of complete treatment, the case half-way off ; (5) admission of clinical data is incomplete, refused to informed consent.

2.3 Treatment

The control group were treated with bronchial artery chemoembolization in the treatment, the specific operation is: first by plain and enhanced CT clear tumor size and blood supply, using modified Selsinger technique for femoral artery puncture, indwelling 5F catheter sheath, the guide wire insertion COOK 5F Cobra catheter, catheterization of bronchial artery, arterial angiography, and to determine whether it is a tumor supply vessel. During the period, avoid the spinal cord, esophagus and intercostal artery; make clear the tumor supply artery. Bronchial artery infusion chemotherapy, super selective Terumo Progreat 3F micro catheter into the artery, through microcatheter slow injecte gemcitabine hydrochloride for Injection (ELI LILLY AND COMPANY, production approval number, H20110535, dosage of 1 000 mg/m^2) and cisplatin (Qi Lu Pharmaceutical Company Limited production, product batch number 20150409, dose 60-90 mg/m^2) chemotherapy after mixing dilution in the fluoroscopy with gelfoam particles after transcatheter embolization. 3 d after the success of bronchial artery embolization in the control group, ^{125}I radioactive particles were implanted in the observation group. Prior to implantation, information about patient data and radioactive particles was entered within the TPS, followed by CT scan to confirm the position, direction, and depth of the needle. Preoperative routine disinfection shop towel, local anesthesia told the patient after breath, after CT scan clear puncture position correct, the needle into the tumor lesions, ^{125}I radioactive particles in 0.5-1.0 cm spacing evenly implanted, the specific implantation program with reference to patients tumor lesion size. After the above operation is completed, the puncture needle is removed for bandaging. Both groups were treated with 21 d as a course of treatment for at least 2 courses.

2.4. Detection indicators

Before treatment and after 2 courses of treatment, all subjects were taken from the fasting peripheral vein blood of 5 mL, and serum levels of tumor markers and T lymphocyte subsets were detected after centrifugation. Serum tumor markers: serum carcinoembryonic antigen (CEA), neuron specific enolase (NSE) and carbohydrate antigen 125 (CA125), detection instrument for automatic electrochemiluminescence assay; T cell subsets including CD4$^+$, CD8$^+$, CD4$^+$/CD8$^+$ and NK cells were detected by flow cytometry, the specific operation strictly in accordance with the operating instructions.

2.5 Statistical analysis

Study on data processing and analysis using SPSS17.0 statistical software, serum tumor markers and T cell subsets were consistent with normal distribution that the two groups before and after treatment group were compared with t test, P<0.05 showed statistically significant.

3. Result

3.1. Comparison of levels of serum tumor markers in two groups

Before treatment, the levels of serum tumor markers CEA, NSE and CA125 between the two groups were not significantly different (P>0.05). The observation group after treatment, CEA, NSE and CA125 were respectively (15.37 ± 9.65) ng/mL, (13.62 ± 1.26) ng/mL and (38.29 ± 6.47) U/mL, were significantly lower than the

Table 1.
Comparison of levels of serum tumor markers in two groups.

Group	n	Treatment time	CEA (ng/mL)	NSE (ng/mL)	CA125 (U/mL)
Control group	45	Before treatment	118.42±19.86	22.85±1.83	132.75±27.93
		After treatment	48.55±10.26*	16.88±1.79*	75.54±9.75*
Observation group	46	Before treatment	119.85±18.72	22.89±2.01	134.58±28.36
		After treatment	15.37±9.65$^{*\#}$	13.62±1.26$^{*\#}$	38.29±6.47$^{*\#}$

Note: Comparison with the same group before treatment, $^*P$<0.05, compare between the group after treatment, $^\#P$<0.05.

Table 2.
Comparison of T cell subsets between two groups.

Group	n	Treatment time	$CD4^+$ (%)	$CD8^+$ (%)	$CD4^+/CD8^+$	NK cell (%)
Control group	45	Before treatment	30.69±4.16	37.68±6.07	1.01±0.27	14.52±1.58
		After treatment	33.41±5.17*	33.87±2.32*	1.19±0.42*	15.95±2.23*
Observation group	46	Before treatment	29.89±4.04	37.31±5.65	1.01±0.36	14.81±1.65
		After treatment	39.42±4.94*#	28.23±3.88*#	1.36±0.27*#	19.03±2.85*#

Note: Comparison with the same group before treatment , *P<0.05, compare between the group after treatment, #P<0.05.

control group after treatment (48.55 ± 10.26) ng/mL, (16.88 ± 1.79) ng/mL and (75.54 ± 9.75) U/mL, the difference was statistically significant (P<0.05); and the two group after treatment, the three indexes were significantly lower than those in the group before treatment, the difference was statistically significant (P<0.05). The results are shown in Table 1.

3.2 Comparison of T cell subsets between two groups

Before treatment, there was no significant difference in T lymphocyte subsets and NK cell levels between the two groups (P>0.05). The control group and the observation group after treatment, $CD4^+$, $CD4^+/CD8^+$ and NK cell levels were (33.41 ± 5.17)%, (1.19 ± 0.42), (15.95 ± 2.23)%, (39.42 ± 4.94)%, (1.36 ± 0.27) and (19.03 ± 2.85)%, compared with the group before treatment. Levels were significantly increased (P<0.05); and after treatment the observation group was significantly higher than the control group, the difference was statistically significant (P<0.05); the observation group after treatment $CD8^+$ level were (28.23 ± 3.88)%, significantly lower than in the group before treatment (P<0.05), and significantly lower than the control group after treatment (33.87 ± 2.32)%, the difference was statistically significant (P<0.05). As shown in table 2.

4. Discussion

Locally advanced non-small cell lung cancer refers to existing mediastinal lymph node metastasis or supraclavicular lymph node metastasis of lung cancer, according to the treatment theory, can be locally advanced non-small cell lung cancer were divided into resectable and unresectable two. Since most patients belong to the stage of stage III above A, they have lost the best time for surgical treatment. Therefore, the clinical treatment is mostly based on systemic comprehensive treatment[7,8]. Relevant guidelines recommend concurrent radiotherapy and chemotherapy, chemotherapy as a standard treatment for locally advanced non-small cell lung cancer, and a large number of studies have confirmed that a certain effect can be achieved[9,10]. But at the same time received radiotherapy and chemotherapy, patients prone to some complications, such as pneumonia, esophagitis, in addition, repeated chemotherapy may lead to vascular tumor cell cell damage, the tumor cells less sensitive to radiation, thereby affecting the overall therapeutic effect[11,12]. Therefore, how to improve the patient's tolerance, reduce the adverse effects of radiotherapy and chemotherapy, and improve the effective dose of radiation is the key to effective treatment of locally advanced non-small cell lung cancer.

Bronchial arterial chemoembolization and radioactive particle implantation are all effective means of treating lung cancer. Bronchial arterial chemoembolization is the use of bronchial arterial drainage of chemotherapy drugs to local tumor tissue, followed by the main artery of the tumor embolization, to inhibit tumor cell DNA synthesis[13]. Related studies have pointed out that bronchial chemoembolization without hemodilution and liver metabolism can directly reach the tumor lesions,the concentration of local chemotherapeutic drugs can be increased to 2-9 times of the original concentration. While the chemotherapeutic drugs act on the local tumor tissue, the drug can also enter the mediastinal lymph node metastasis lesions, and the metastasis tumor can directly kill the tumor, and finally achieve the purpose of reducing the malignant degree[14,15]. The long half-life of ^{125}I radioactive particles, to local tumor tissue after implantation, mainly through the continuous emission of low energy gamma rays radiotherapy of tumor cells, play an uninterrupted radiotherapy effect, through the radiation biological effects, making the tumor tissue cell damage, reproductive capacity loss, abnormal metabolic disorders. Thereby promoting the aging of tumor cells and death, enhance the ability to kill tumor cells. Related studies have suggested that the combined use of two methods in the treatment of locally advanced non-small cell lung cancer can achieve a certain effect, and less adverse reactions occurred[16].

The occurrence and development of malignant tumors are closely related to the immune function of the body. Autoimmune dysfunction is one of the important factors for tumor cell expansion[22]. Immune function plays an important role in the defense and elimination of tumor, and T lymphocyte is the main functional cell of anti-tumor. Most of the patients with malignant tumor were in immunosuppressive state. The clinical manifestations showed that the levels of $CD4^+$ and $CD4^+/CD8^+$ decreased, and the number of $CD8^+$ cells increased significantly. With the aggravation of tumor severity, the level changes of cells were more obvious[23]. NK cells are natural killer cells, which can kill some tumor cells directly, and decrease their number (activity) level, which can directly lead to the decrease of anti-tumor ability of the organism[24]. The results of this study found that after bronchial artery embolization and radioactive seed implantation, the $CD4^+$, $CD4^+/CD8^+$ levels and NK cells number in patients were significantly increased, $CD8^+$ level decreased significantly, the results reveal that the two therapies can improve the immune function of the patients, the level of T cells in patients with normal, but also indirectly reflects reduced in patients

with malignancy. The results show that the combination of the two therapies can further improve the immune function of the patients, make the T cell level tend to normal, and indirectly reflect the reduction of the malignancy of the patients.

In summary, bronchial arterial chemoembolization combined with radioactive particles implantation in the treatment of locally advanced non-small cell lung cancer can effectively play a synergistic effect of the two treatments, which can further reduce the degree of tumor deterioration, effectively reduce the serum tumor marker level, to improve the level of T cells, has important clinical value.

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