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Clinical analysis of acute cerebral infarction accompanied with lung cancer

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ABSTRACT

Objective: To analyze the characteristic of coagulation function in non-small cell lung cancer patients with acute cerebral infarction as the initial symptom.
Methods: Cases diagnosed as non-small cell lung cancer in our hospital from January 2015 to January 2016 were used for study. Fifteen cases with acute cerebral infarction as the initial symptom were included in experimental group. Thirty-three cases with no initial symptom on acute cerebral infarction were included in control group. Clinical data in patients of two groups were collected, including general information, coagulation function index, thrombelastogram index.
Results: The prothrombin time (PT) [(9.69 ± 1.42) *vs.* (13.04 ± 1.96) s], activated partial thromboplastin time (APTT) [(30.14 ± 5.79) *vs.* (39.34 ± 7.63) s], international normalized ratio (INR) [(0.76 ± 0.10) *vs.* (1.35 ± 0.22)], coagulation reaction time (R) [(4.76 ± 0.79) *vs.* (6.11 ± 0.93) min], and blood clot formation time (K) [(1.73 ± 0.21) *vs.* (6.11 ± 0.93) min] in patients of experimental group were obviously lower than that of in control group. Fibrinogen (FIB) [(5.43 ± 0.89) *vs.* (2.14 ± 0.36) g/L], D-dimer [(0.84 ± 0.17) *vs.* 0.30 ± 0.06) mg/L], the maximum amplitude of thrombus (MA) [(65.62 ± 10.34) *vs.* (48.69 ± 8.61) mm], and α-angle [(68.12 ± 9.51) *vs.* (60.37 ± 10.29) deg] in patients of experimental group were obviously higher than that in control group. PT, APTT, INR, R value, and K value in patients of tumor node metastasis (TNM) Stage III–IV were significantly lower than that in TNM Stage I–II, and FIB, D-dimer, MA, α-angle were all higher than that in patients of TNM Stage I–II. PT, APTT, INR, R value, K value in patients with lymphatic metastasis were significantly lower than that in patients with no lymph node metastasis, and FIB, D-dimer, MA, α-angle were obviously higher than that in patients with no lymph node metastasis.
Conclusions: Patients with non-small cell lung cancer have hypercoagulability and hyperfibrinolysis with acute cerebral infarction as the initial symptom, and coagulation function involved in the development of lung disease.

1. Introduction

Lung cancer is one of the most malignant tumors worldwide. The occurrence rate and case fatality rate of lung cancer in our country are rising in recent year[1,2]. Non-small cell lung cancer is the most common type of lung cancer, which accounts for over 90% of all lung cancers. Patients are lack of clinical symptom in the early stage, and most patients have been developed to advanced stage at the time of diagnosis, and its prognosis conditions is relatively worse. Although the new targeted drug and chemotherapy drug are constantly developing, the survival rate is still very low[3–6]. Some studies have proved that blood in abnormal hypercoagulability state and the abnormal of coagulation function will increase the risk of arterial embolism in the disease progresses of non-small cell lung cancer[7,8]. Acute cerebral infarction is the initial symptom for some patients with lung cancer, and the existence of lung malignancies was found in the process of diagnosis and treatment of cerebral infarction[9,10]. At present, fewer researches have been done on lung cancer patients with acute cerebral infarction as the initial symptom, and also lack of understanding on this kind of clinical features. Correctly understand the changes of coagulation function in the pathogenic process of lung cancer not only help to early predict the occurrence risk of cerebral infarction and prevent the occurrence of cerebral infarction, but

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also provide the basis for early diagnosis and screening of lung cancer. In this study, we analyzed the clinical features of acute cerebral infarction accompanied with lung cancer.

2. Materials and methods

2.1. Case data

Cases diagnosed as non-small cell lung cancer in our hospital from January 2015 to January 2016 were selected in this study. Inclusion criteria: age >18 years; patients were diagnosed as non-small cell lung cancer by biopsy pathology; patients were the first time diagnosis and received no anti-cancer treatment before, and have complete clinical data. Exclusion criteria: patients were diagnosed as other types of lung cancer; patients once received the anti-cancer therapies of radiotherapy, chemotherapy, and targeted therapy, *etc.*; patients involved the presence of distant metastases, and had the medical history of ischemic stroke. Patients with acute cerebral infarction as the initial symptom conformed to the diagnostic criteria of acute cerebral infarction in the Fourth National Conference on Cerebrovascular Disease (1995)[11]. New infarction lesions can be explained by using head CT scan to exclude hemorrhage, as well as using skull magnetic resonance imaging scanning and diffusion weighted imaging to confirm the occurrence of long T1, long T2 and high diffusion weighted imaging signals in head.

2.2. Collection methods of clinical information

Case data were conducted with retrospective analysis for patients. General data including gender, age, body mass index (BMI) index, tumor node metastasis (TNM) staging, lymphatic metastasis. Analytical methods of coagulative function index: after taking peripheral blood, coagulation analyzer was used to detect prothrombin time (PT), activated partial thromboplastin time (APTT), international normalized ratio (INR), fibrinogen (FIB), and D-dimer. Thrombelastogram analytical methods: TEG-500 thromboelastography (Haemoscope Company, Hong Kong) was used to detect the maximum amplitude of thrombus (MA), coagulation reaction time (R), blood clot formation time (K), and blood clot formation rate (α-angle).

2.3. Statistical analysis

Data were inputted and analyzed by SPSS version 19.0. Measurement data was expressed by mean ± SD, and *t*-test was used for the analysis between two groups. Enumeration data were expressed by frequency and analyzed by *Chi*-square test. $P < 0.05$ was considered as statistical significance.

3. Results

3.1. General data in patients of two groups

Among the patients with non-small cell lung cancer, 15 cases of acute cerebral infarction as the initial symptom were included in experimental group. Thirty-three cases with no acute cerebral infarction as the initial symptom were included in control group. In experimental group, 10 cases were males and 5 cases were females, with mean age of (58.0 ± 7.0) years, BMI [(22.1 ± 4.5) kg/m^2], 3 cases in TNM Stage I, 5 cases in Stage 2, 5 cases in Stage III, 2 cases in Stage IV, 4 cases in lymphatic metastasis. In control group, 23 cases were males, and 10 cases were females, with mean age of (55.0 ± 8.0) years, BMI [(21.3 ± 4.9) kg/m^2], 6 cases in TNM Stage I, 10 cases in Stage II, 12 cases in Stage III, 5 cases in Stage IV, 9 cases in lymphatic metastasis. According to statistic analysis, gender, age, BMI index, TNM staging, and lymphatic metastasis in patients of experimental group have no difference with patients in control group (Table 1).

Table 1
General data in patients of two groups.

General data	Experimental group (n = 15)	Control group (n = 33)	P
Gender (male/female)	10/5	23/10	> 0.05
Age (year)	58.0 ± 7.0	55.0 ± 8.0	> 0.05
BMI (kg/m^2)	22.1 ± 4.5	21.3 ± 4.9	> 0.05
TNM staging (I/II/III/IV)	3/5/5/2	6/10/12/5	> 0.05
Lymphatic metastasis	4	9	> 0.05

3.2. Coagulation function in patients of two groups

PT, APTT, INR, R, and K in patients of experimental group were obviously lower than that of in control group. FIB, D-dimer, MA, and α-angle in patients of experimental group were significantly higher than that of in control group (Table 2).

Table 2
Coagulation function in patients of two groups.

Parameters	Experimental group (n = 15)	Control group (n = 33)	P
PT (s)	9.69 ± 1.42	13.04 ± 1.96	< 0.05
APTT (s)	30.14 ± 5.79	39.34 ± 7.63	< 0.05
INR	0.76 ± 0.10	1.35 ± 0.22	< 0.05
FIB (g/L)	5.43 ± 0.89	2.14 ± 0.36	< 0.05
D-dimer (mg/L)	0.84 ± 0.17	0.30 ± 0.06	< 0.05
MA (mm)	65.62 ± 10.34	48.69 ± 8.61	< 0.05
R (min)	4.76 ± 0.79	6.11 ± 0.93	< 0.05
K (min)	1.73 ± 0.21	2.48 ± 0.34	< 0.05
α-Angle (deg)	68.12 ± 9.51	60.37 ± 10.29	< 0.05

3.3. Coagulation function in patients of experimental group in different TNM staging

PT, APTT, INR, R, K in patients of TNM Stage III–IV were obviously lower than that of in patients of TNM Stage I–II. FIB, D-dimer, MA, α-angle in patients of experimental group were significantly higher than that of in patients of TNM Stage I–II (Table 3).

Table 3
Coagulation function in patients of experimental group in different TNM staging.

Parameters	TNM stage I–II (n = 8)	TNM stage III–IV (n = 7)	P
PT (s)	12.13 ± 1.98	7.24 ± 1.03	< 0.05
APTT (s)	35.25 ± 6.94	29.14 ± 5.88	< 0.05
INR	0.98 ± 0.13	0.61 ± 0.09	< 0.05
FIB (g/L)	3.98 ± 0.67	6.23 ± 0.72	< 0.05
D-dimer (mg/L)	0.59 ± 0.11	1.09 ± 0.23	< 0.05
MA (mm)	55.34 ± 8.92	71.34 ± 12.35	< 0.05
R (min)	5.23 ± 0.84	3.24 ± 0.56	< 0.05
K (min)	2.04 ± 0.32	1.39 ± 0.18	< 0.05
α-Angle (deg)	63.36 ± 8.22	74.10 ± 11.28	< 0.05

3.4. Coagulation function in patients of experimental group in different lymphatic metastasis conditions

PT, APTT, INR, R, K in patients with lymphatic metastasis were obviously lower than that of in patients with on lymphatic metastasis. FIB, D-dimer, MA, α-angle in patients of experimental group were significantly higher than that of in patients with lymphatic metastasis (Table 4).

Table 4
Coagulation function in patients of experimental group in different lymphatic metastasis conditions.

Parameters	No lymph node metastasis (n = 11)	Lymphatic metastasis (n = 4)	P
PT (s)	13.94 ± 2.12	6.03 ± 0.91	< 0.05
APTT (s)	36.61 ± 6.52	27.83 ± 6.12	< 0.05
INR	1.06 ± 0.15	0.55 ± 0.07	< 0.05
FIB (g/L)	4.03 ± 0.79	6.03 ± 0.67	< 0.05
D-dimer (mg/L)	0.51 ± 0.10	1.20 ± 0.28	< 0.05
MA (mm)	51.61 ± 8.35	75.16 ± 11.18	< 0.05
R (min)	5.61 ± 0.78	3.03 ± 0.52	< 0.05
K (min)	2.11 ± 0.33	1.32 ± 0.16	< 0.05
α-Angle (deg)	62.12 ± 8.41	75.22 ± 10.85	< 0.05

4. Discussion

States of hypercoagulability and hyperfibrinolysis in patients with malignant tumor has received more and more attentions in recent years. Hypercoagulability and hyperfibrinolysis will increase the occurrence risk of embolism in artery thrombosis, causing the increasement of occurrence rate in myocardial infarction, cerebral infarction and other disease[12–15]. Some patients show acute cerebral infarction and myocardial infarction as the initial symptoms before they were diagnosed as malignant tumor, in which some of these patients have already developed into middle and advanced stage of tumour and the lymphatic metastasis has been made[16–18]. At present, corresponding research and cognition are deficient in the clinical features of lung cancer patients with acute cerebral infarction as the initial symptoms. Among patients with non-small cell lung cancer in this study, 15 cases of acute cerebral infarction were set as the initial symptoms, in which the proportion of advanced malignant tumor was 7/15, 4/15 in lymphatic metastasis, suggesting that most patients show acute cerebral infarction as the initial symptom before diagnosing as the non-small cell lung cancer, and patients in middle and advanced stage and lymphatic metastasis occupied the certain proportion in this part of patients.

PT and APTT mainly reflected the content and function of various blood coagulation factors in endogenous and exogenous coagulation system. Endogenous coagulation pathway can be activated when blood contact with negative foreign material on its surface. Exogenous coagulation pathway can be activated when tissue factors trigger cascade reaction[19–21]. Prolonged APTT and PT are the main performance of body hypercoagulability. Besides, hyperfunction of fibrinolytic system is another performance of body hypercoagulability. Fibrinogen and D-dimer are the specific indexes of reflecting fibrinolytic system activity. Fibrinogen was originally synthesized with liver, after being activated, it transforms into fibrinogen polymer cross-linking of various hemocyte to form blood clot[22,23]. D-dimer is the product of cross-linked fibrin after cleavage, which can reflect the formation and degradation degree of fibrin[24,25]. We analyzed the coagulation function index in non-small cell lung cancer patients with acute cerebral infarction as the initial symptom, discovering that APTT and PT in patients of experimental group were obviously lower than of in control group, and fibrinogen and D-dimer were significantly higher than that of in control group, which indicated that lung cancer with acute cerebral infarction as the initial symptom has hypercoagulability and hyperfibrinolysis.

Thrombelastography is a newly developed adjuvant diagnostic method for testing aggregation, coagulation and fibrinolysis of platelet, which can reflect the content and function of blood coagulation factor, fibrinogen and blood platelet to further access the coagulation and fibrinolytic statuses of body[26,27]. R value and K value are the coagulation reaction time and formation time of blood clot respectively to reflect the formation velocity of sludged blood and steady the formation time of sludged blood, which mainly related to the content of fibrinogen and activity of platelet[28]. α-Angle, also called as coagulation angle, representing the formation rate of blood clot, which is influenced by the content of fibrinogen and activity of platelet[29]. MA reflects the strength and stability of sludged blood after the formation that mainly impacted by the platelet aggregative function[30]. We analyzed the coagulation function index in non-small cell lung cancer patients with acute cerebral infarction as the initial symptom, discovering that R value and K value in patients of experimental group were shorter than of in control group, and MA and α-angle were greater than that of in control group, which indicated that lung cancer patient with acute cerebral infarction as the initial symptom has higher content of fibrinogen, activity of platelet and stronger aggregation function, and the overall performance showed hypercoagulability.

In the development process of disease of non-small cell lung cancer, correctly understand the change condition of coagulation function can not only benefit for early predict the occurrence risk of cerebral infarction and prevent the occurrence of cerebral infarction, but also provide the basis for early diagnosis and screening of lung cancer. In order to define the relationship between the change of coagulation function and the occurrence and development of lung cancer, we analyzed the influence of different TNM staging on coagulation function. Results showed that PT, APTT, INR, R value, and K value in patients of TNM Stage III–IV were significantly lower than that of in patients of TNM Stage I–II. This reflects the development of lung disease accompanied by changes of coagulation. On this basis, further analysis of the influence of lymph node metastasis status on coagulation function can conclude that PT, APTT, INR, R value and K value in patients with lymphatic metastasis were significantly lower than that of in patients with non lymph node metastasis, and FIB, D-dimer, MA and α-angle were significantly higher than that of in patients with non lymph node metastasis. It was concluded that the changes of coagulation function in patients with lung cancer related to the metastasis of lymphonodus.

In conclusion, non-small cell lung cancer patients with acute cerebral infarction as the initial symptom have hypercoagulability and hyperfibrinolysis, and its the coagulation function was associated with the development of lung cancer.

Conflict of interest statement

The authors report no conflict of interest.

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