APPLICATION VALUE OF JOINT DETECTION OF SERUM MARKER CYFRA21-1, NSE, CEA, CA19-9, CA125, SCC IN DIAGNOSIS OF LUNG CANCER

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ABSTRACT

Introduction: To further increase diagnosis accuracy of lung cancer and seize the optimal opportunity for treatment, in this paper we conducted in-depth analysis on application value of joint detection of CYFRA21-1, NSE, CEA, CA19-9, CA125 and SCC in diagnosis of lung cancer.

Materials and methods: In this research, 1000 patients, who have been clinically diagnosed with lung cancer, were selected into observation group, in which there were 312 patients of small cell carcinoma, 458 with adenocarcinoma, and remaining 330 with squamous carcinoma. In addition, 200 healthy people were selected as research objects in control group. Electrochemistry luminescence method was adopted to test index levels of the two groups, respectively, with test items including CYFRA21-1, NSE, CEA, CA19-9, CA125, SCC.

Results: Test results showed the serum indexes of observation group were significantly higher than those of control group. In addition, through comparing 3 different types of lung cancer patients, patients with small cell carcinoma had a significantly higher concentration of serum NSE than those with squamous carcinoma or adenocarcinoma; the concentrations of CA125, CEA, CA19-9 in patients with adenocarcinoma were higher than that of patients with squamous carcinoma or small cell carcinoma; the concentrations of CYFRA21-1 in patients with squamous carcinoma was the highest of the three. Moreover, it finally confirmed 958 lung cancer patients in total by testing 6 serum indexes of all selected patients, with positive rate accounting for 87.09%.

Conclusion: As a result, it is of vital significance to test serum indexes such as CYFRA21-1, NSE, CEA, CA19-9, CA125, SCC for suspected lung cancer patients, and the concentrations of different indexes play key roles in confirming type of lung cancer. Finally, it concluded that joint detection of serum markers can further enhance diagnosis efficiency, which should be promoted in clinical practice.

Keywords: Serum Marker, Diagnosis of Lung Cancer, Chemiluminescence Detection, Application Value.

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Introduction

With the fastest growth of morbidity and mortality rates, lung cancer is one of most threatening cancers to people's health and life (See Fig.1)\(^5\). Due to the increasingly worsening environment pollution over the past 5 decades, many countries have reported significantly increased morbidity and mortality rates of lung cancer, wherein male lung cancer patients suffer the top morbidity and mortality rates compared with patients with other cancers, female lung cancer patients suffer the second highest morbidity rates and mortality rates. To reduce mortality rate caused by lung cancer, it is suggested to receive treatment as soon as possible\(^5\).

Since lung cancer has complex types and insignificant early symptoms, it is difficult to confirm the disease timely. During routine examination, patients are normally applied with histopathological and cytological examination.
However as these examination methods are relatively complex, the examination accuracy cannot be guaranteed. In recent years, there have been some documents reporting that examining lung cancer with tumor markers can confirm the exact type of lung cancer as soon as possible, so as to provide scientific guidance reference for clinical treatment(3). Tumor marker is resulted from malignant cells disorder or during host’s response to stimulation of tumor. Tumor marker can reflect emergence and development of tumor, and monitor tumor’s response to treatment as well(4). Tumor marker exists in tissue, body fluid, and excreta of cancer patients, and can be detected by immunological, biological, and chemical detection method.

To prove such conclusion, we selected 1100 patients with different types of lung cancers as research objects in this research, and performed joint detection of CYFRA21-1, NSE, CEA, CA19-9, CA125, SCC using photochemical detecting method.

Materials and methods

General data

From March 2015 to March 2016, we selected from 20 hospitals 1100 lung cancer patients as research objects and put them in observation group. Pathological and iconographical examining results showed that there were 312 patients with small cell carcinoma, 458 with adenocarcinoma, and 330 with squamous carcinoma. Of all researched objects in observation group, there were 724 male patients and 358 female ones, with age ranging from 34 to 81 years old (averages at 48.7±7.3).

On the other hand, we selected 200 healthy people, who accepted examination from the same hospitals and during the same period of time, as research objects for control group, in which there were 117 male patients and 83 female ones, with age ranging from 25 to 72 years old (averages at 47.6±7.2).

Detection method

Serums of patients in both groups were analyzed with chemi-luminescence detection. Before blood sampling, all selected patients should be maintained in fasting state, and then their venous blood was collected for separating serums including CYFRA21-1, NSE, CEA, CA19-9, CA125, SCC. For this test, the automatic UniCel DxI 800 chemical luminescence immunity analyzer from Beckman Coulter Co., Ltd. was adopted, and relevant reagents were auxiliary product from the same company. Samples were first combined with related antibodies which had been wrapped in fine particle, and then combined with acridinium ester labeled antibodies to form compounds(5). Particulate compounds were absorbed by magnet on wall of reacting cup. After washing off uncombined materials, pre-activating fluid and activating fluid were added, so that N-methylacridone can be produced and energy (light emission) was released. Analyte concentration can be calculated according to chemiluminescence emission amount (i.e. the reading).

CYFRA21-1 and NSE were detected using ELECSYS 2010 electrochemistry luminescence immunity analyzer from Roche Inc., and the regents used in this test were also from the Roche Inc. To guarantee the detection accuracy, all detection personnel should operate in accordance with the requirements. Samples were combined with related antibodies which had been wrapped in fine particles, and then combined with enzyme-labeled antibodies to for compounds(6). Particulate compounds were inevitably harvested by fiberglass at bottom of cuvette, and enriched on its surface. Fluorogenic substrate 4-MUP was decomposed by alkaline phosphatase into MU which produced fluorescence under the irradiation of 360nm exciting light. According to fluorescence intensity, we calculated the concentration of NSE.

Clinical observation indexes

Both groups were applied with chemiluminescence detection, with the same serum markers being detected.

The standard ranges for serum markers are shown below: CYFRA21-1>3.3ng/ml, NSE>15.2ng/ml, CEA>5.0ng/ml, CA19-9>37.0ng/ml, CA125>35.0ng/ml, SCC>1.5ng/ml. Positive results can be confirmed if detected results are out of standard range.

The 1100 lung cancer patients were categorized according to existing types of lung cancer. The aver-
Age concentration of each serum marker was calculated, and then compared with that of control group.

**Statistic method**

Regarding the study on application value of joint detection of CYFRA21-1, NSE, CEA, CA19-9, CA125 and SCC in diagnosis of lung cancer, Statistical Product and Service Solutions (SPSS)19.0 statistical software was adopted for analysis and processing of related data. Enumeration data was expressed in form of (n, %), and tested via chi-square; while measurement data was expressed in form of (x±s), and tested via t. Only when P<0.05 was met, can the differences be regarded of statistical significance.

**Results**

The concentrations of all serum markers of observation group were significantly higher than those of control group, wherein CYFRA21-1 concentration was 7.13±8.24 ng/ml, NSE concentration was 29.78±28.67 ng/ml, CEA concentration was 67.54±287.46 ng/ml, CA19-9 concentration was 112.43±343.17 ng/ml, CA125 concentration was 123.64±423.55 ng/ml, SCC concentration was 2.87±9.46 ng/ml. Compared with control group in term of each serum marker concentration, it can always reach P<0.05, with statistic significance.

In addition, compared patients with 3 different types of lung cancers, it can find that CEA concentration of patient with small cell carcinoma (see Fig. 2) was 11.37±26.24 * 10ng/ml, which was significantly higher that of patients with squamous carcinoma or adenocarcinoma.

In addition, concentrations of CA125 and CA19-9 in patients with adenocarcinoma (see Fig. 3) were 20.87±46.74 * 10ng/ml and 16.89±43.72 * 10ng/ml, respectively, which were significantly higher than that of patients with squamous carcinoma or small cell carcinoma.

Concentrations of CYFRA21-1, NSE, CEA, CA19-9, CA125 and SCC in patients with squamous carcinoma (see Fig. 4) were 8.43±12.56 * 10ng/ml, 30.74±32.17 * 10ng/ml, 3.76±9.46 * 10ng/ml, respectively, which were the highest of the three. Through comparing the concentrations of all serum markers, it can always reach P<0.05, with statistic significance.

**Discussion**

According to research results of this paper, it can find that lung cancer patients have significantly higher concentrations of 6 cancer markers including CYFRA21-1, NSE, CEA, CA19-9, CA125 and SCC as compared with healthy people. In addition, of all patients with 3 different types of lung cancers including small cell carcinoma, squamous carcinoma and adenocarcinoma, the concentrations of the 6 cancer markers also varied among the 3 types of lung cancers. Therefore, it can conclude the detection of concentrations of different cancer markers plays a significant role in diagnosing the type of lung cancer.

As a soluble fragment of cytokeratin 19, CYFRA21-1 has become one of the most significant indexes for diagnosis of cancer. However, the possibility of cancer still cannot be ruled out even though CYFRA21-1 is detected to be negative.
Reports show that the sensitivity of CYFRA21-1 to diagnosis of different types of lung cancers can be sequenced as: squamous carcinoma > adenocarcinoma > large cell carcinoma > small cell carcinoma (7).

Serum NSE is a specific acid protease in neuron and neuroendocrine cell. In the process of human cell transforming from normal to malignant, metabolism results lead to change of glycoproteins and glycolipids on cell surface, which is reflected by glyco-gen increase on cancer cell. Clinically-proven results show that 60-81% of all small cell lung cancer patients suffer increased concentration of serum NSE, therefore, it is of great significance to lung cancer diagnosis as well as to evaluation of treatment effect.

As a glycoprotein produced from colorectal cancer tissue, CEA, as an antibody, can trigger immune response. CEA, as a wide-adaptability cancer marker, can reflect existence of multiple cancers. However, due to poor specificity and insufficient sensitivity, it is not suitable for single detection. CA125 is a glycoprotein, which is detected from epithelial ovarian cancer antibody and can be combined with monoclonal antibody OC125. CA125 derives from coelomic epithelium during embryonic development period and does not exist in normal ovarian tissue.

Therefore, it is most often found in epithelial ovarian tumor (in patient’s serum), with higher sensitivity but poorer specificity (8). SCC is a glycoprotein which is extricated from squamous epithelial stromal cancer tissue of cervix, with sound specificity. However as half-life period of SCC is relatively short, it is not suitable for single detection either (9-10).

In all, this paper proves that the 6 cancer markers are all of great values to clinical diagnosis of lung cancer. Considering the certain limitation of single index detection, it is suggested to conduct joint detection to confirm the disease and give treatment as soon as possible, and thus realizing the purpose of saving lives and improving living quality.

References
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