RESEARCH ARTICLE

Clinical Observations on the Association Between Diagnosis of Lung Cancer and Serum Tumor Markers in Combination

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Abstract

Objective: To evaluate the association of a diagnosis of lung cancer and combined detection of serum carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA19-9), neuron specific enolase (NSE) as well as the cytokeratin 19 fragment (CYFRA21-1). Methods: Serum CEA, CA19-9, NSE and CYFRA21-1 were assessed in 150 patients with lung cancer, 100 patients with benign lung disease and 100 normal control subjects, and differences of expression were compared in each group, and joint effects of these tumor markers in the diagnosis of lung cancer were analyzed. Results: Serum CEA, CA19-9, NSE and CYFRA21-1 in patients with lung cancer were significantly higher than those with benign lung disease and normal controls (p<0.01). It is suggested that these four tumor markers combined together could produce a positive detection rate of 90.2%, significantly higher than that of any single test. Conclusion: Combination detection of CEA, CA19-9, NSE and CYFRA21-1 could significantly improve the sensitivity and specificity in diagnosis of lung cancer, and could be important in early detection.

Keywords: Lung cancer - CEA - CA199 - NSE - CYFRA21-1

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Introduction

Lung cancer is one of the most common malignant tumors, with high mortality rate worldwide, and still demonstrating a rising trend yearly (Parkin et al., 2005; Liu et al., 2013; Lu et al., 2013). In China, lung cancer is more common than stomach and liver cancer, and is the first cause of death from malignant tumors (Hu et al., 2013). However, conventional diagnostic methods, eg., imaging, fiber bronchoscope, cytology and histopathologic is difficult for early detection of lung cancer (Malik et al., 2013). Recently, tumor markers is suggested to be a usefull tool in this setting, especially in early diagnosis of lung cancer (Buccheri et al., 2002; Schneider et al., 2002; Kav et al., 2012). On this background, we developed a method of joint detection of serum carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA19-9), neuron specific enolase (NSE) as well as cytokeratin 19 fragment (CYFRA21-1). The current study is to test our hypothesis that this method is superior to conventional methods.

Materials and Methods

Study subjects

From March 2011 to February 2013, 150 patients with lung cancer were retrospectively recruited. Among these patients 89 were male, 61 were female; aged 38-69 years, average 54.8 years. All lung cancer patients were by pathologically or cytologically confirmed. Patients with lung benign disease were diagnosed with pulmonary tuberculosis, pneumonia and bronchiectasis, totally 100 patients. Among these patients with non-cancer benign disease, 58 were male, 42 female, aged 24 to 72 years. Control group was consisted by 100 subjects (59 male and 41 female, aged 9-22 years) who underwent healthy physical examination.

Study materials and methods

Peripheral morning fasting blood were obtained from all study subjects. To isolate serum for subsequent testing, centrifugation was set as 2000 turn/RPM for 15 minutes. Chemiluminescence immunoassay was used to electrochemically detect CEA, CA19-9, NSE and CYFRA21-1, and all experiment operating was in strict accordance with the instructions authorised by instrument and reagent kit.

Evaluation

Negative testing was set if CEA < 5.0 ng/ml, CA19-9 < 37 U/ml, NSE < 15.0 ng/ml, and CYFRA21-1 < 3.3 ng/ml, otherwise positive if specimen serum tumor markers detected equal to or greater than the upper limit of above mentioned value.

Statistical analysis

SPSS13.0 statistical software was used for statistical analysis. Enumeration data was expressed as \( \bar{x} \pm s \);
Tumor markers, that are produced by tumor cells, are useful tools in the diagnosis of lung cancer, and can be an indicator for monitoring curative effect as well as prognosis for patients with lung cancer. This study suggests that a number of tumor markers might be associated with lung cancer, and a single test could result in misdiagnosis. Therefore, our purpose is to develop a diagnostic system to improve sensitivity, and specificity on lung cancer screening.

At present CEA is mainly used in the diagnosis of gastrointestinal cancer, however, it is reported that the sensitivity of CEA is around 35% to 77% (Ramshankar et al., 2013), our study suggested that the sensitivity of CEA in detecting lung cancer was 39.45%, and the specificity was 73.53%, that is in accordance with previous reports. Another finding of our study is that serum CEA in patients with lung cancer were significantly higher than those with benign disease and healthy controls (p < 0.05), indicating that CEA could be used in early diagnosis of lung cancer.

CA19-9 tumor associated antigen is commonly used in patient with pancreas, liver, and colorectal cancers. Now, it is confirmed that CA199 is an important marker in diagnosis of lung cancer, and the sensitivity in detecting lung cancer was 43.76%, specificity was 78.34% (Bilgin et al., 2013). In this study, serum CA199 in patients with lung cancer were significantly higher than those with benign disease and healthy controls (p < 0.05), indicating that CA199 is of importance in the diagnosis of lung cancer.

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were significantly higher than those with lung benign disease and healthy controls (p< 0.05), suggesting that it is important in the diagnosis of lung cancer, especially small cell lung cancer.

Clinical and pathological research found that lung cancer is heterogeneous (Oguz et al., 2013). To improve the diagnostic sensitivity and specificity, several tumor markers, combined together could be more effective in the diagnosis of lung cancer. Our results showed that CEA, CA19-9, NSE and CYFRA21-1 as a single detection of lung cancer, CYFRA21-1 is a marker bearing the highest sensitivity with positive rate of 58.42%. When CEA, CA199 and CYFRA21-1 combined together, the sensitivity was 86.67%, and specificity 83.24%; instead, if CEA, CA199 and NSE combined together, the sensitivity was 76.28%, specificity 79.61%; most high sensitivity was 90.16% after a joint of CEA, CA199,NSE and CYFRA21-1 together, and the specificity was 75.64%.

In summary, single measurement of CEA and CA19-9, CYFRA21-1 and NSE is of diagnostic value in the diagnosis of lung cancer, and a joint detection of these four tumor markers, could greatly improve the sensitivity of diagnosis on lung cancer. Thus is helpful for the differential diagnosis of lung cancer and lung benign disease. However, this method should be confirmed by further randomized clinical trials.

References


