Researches on the diagnosis value of tumor markers combined detection to middle-aged patients with pulmonary tuberculosis complicating lung cancer

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ABSTRACT

Objective: To discuss the diagnosis value of six kinds of tumor markers (CEA, NSE, CYFRA21-1, CA125, CA199, AFP) combined detection to middle-aged patients with pulmonary tuberculosis complicating lung cancer. Methods: A total of 52 cases with pulmonary tuberculosis complicating lung cancer who were admitted in our hospital between January 2014 and April 2015 were selected as A Group and 76 cases with pulmonary tuberculosis were selected as B Group, and 118 cases with physical examination during the corresponding period were selected as C Group. Tumor markers (CEA, NSE, CYFRA21-1, CA125, CA199 and AFP) levels of patients in each group were detected. Results: CEA, NSE, CYFRA21-1, CA125, CA199 and AFP levels of patients in A Group were (17.56±8.38) g/L, (40.12±5.22) ng/mL, (7.32±2.41) g/L, (53.27±10.26) U/mL, (41.26±9.41) U/mL and (24.17±9.46) ng/ml respectively, which was significantly higher than that in B Group and C Group, and difference had statistical significance; comparative difference of tumor markers levels between B Group and C Group had no statistical significance; CEA and CYFRA21-1 levels of patients with small cell lung cancer in A Group were (26.32±9.16) g/L and (11.47±2.18) g/L respectively, which was significantly higher than those patients with non-small cell lung cancer, but NSE level was (15.17±5.91) ng/mL, which was lower than those patients with non-small cell lung cancer; comparative difference of CA125, CA199 and AFP levels between small cell lung cancer patients and non-small cell lung cancer patients had no statistical significance; sensitivity of CEA was the highest (50.00%), specificity of CA199 was the highest(91.24%). Sensitivity of 6 kinds of tumor markers combined detection was 71.15%, and specificity was 89.69%. Conclusion: CEA, NSE, CYFRA21-1, CA125, CA199 and AFP combined detection had a certain clinical value for the diagnosis of pulmonary tuberculosis complicating lung cancer.

1. Introduction

Along with the increasing number of aging population in our country, pulmonary tuberculosis complicating lung cancer patients were significantly increasing accordingly. Chest radiography and chest CT imaging performance of early stage pulmonary tuberculosis complicating lung cancer patients had no obvious specificity, which was difficult to differ from pure pulmonary tuberculosis[1,2]. In recent years, extensive application of serum tumor markers has obviously improved the early stage positive diagnosis levels of malignant tumor patients. Some scholars believed that except for that CEA, CA125, CA199, AFP levels of Peripheral Blood were obviously increased in lung cancer patients and pulmonary tuberculosis complicating lung cancer patients, NSE and CYFRA21-1 levels were obviously increased in lung cancer patients, especially in pulmonary tuberculosis complicating lung cancer patients[3,4]. In this study, 52 cases with pulmonary tuberculosis complicating lung cancer who were admitted in our hospital between January 2014 and April 2015 were selected as A Group and 76 cases with pulmonary tuberculosis were selected as B Group, and 118 cases with physical examination during...
the corresponding period were selected as C Group, and we have detected the relevant tumor markers of Peripheral Blood of patients in each group, in order to develop the potential value of combined detection. The detailed research results were as followed:

2. Data and Methods

2.1. General Data

A total of 52 cases with pulmonary tuberculosis complicating lung cancer who were admitted in our hospital between January 2014 and April 2015 were selected as A Group, with male/female cases 30/22 cases, average age (56±8) years old and 76 cases with pulmonary tuberculosis were selected as B Group, with male/female cases 47/29 cases, average age (56±8) years old and 118 cases with physical examination during the corresponding period were selected as C Group, with male/female cases 72/46 cases, average age (56±10) years old. Inclusion criteria: (1) Cases were confirmed by pathology, imageology and sputum culture diagnosis; (2) Karnofsky scoring was (15.17±5.91) ng/mL, which was lower than that (43.18±4.82) ng/mL of non-small cell lung cancer patients, however, NSE was(17.56±8.38) g/L, (40.12±5.22) ng/mL, (7.32±2.41) μ g/L, (53.27±10.26) U/mL, (41.26±9.41) U/mL and (24.17±9.46) ng/mL respectively, which was significantly higher than that in B group and C group, and difference had statistical significance (P<0.05); CA125, CA199 and AFP comparative difference of tumor marker levels between B group and C group had no statistical significance (P>0.05). As was shown in Table 1.

2.2. Detection Method

4 mL of morning fasting blood of all cases was collected and then serum was separated and was stored in -4 ℃ freezer. Cobas e411 fully automatic immunochemistry analyzer produced by Roche Group, and related supplementary reagents (CEA, CA125, CA199, AFP, NSE and CYFRA21-1) produced by Nanjing Keygen Biotech. Co. , Ltd. were used for relevant tumor markers detection. Detection method was macroparticle euzymelinked immunosorbent assay.

2.3. Detection Standard

Normal reference value of each detection items: CEA<7 g/L, NS13 ng/mL, CYFRA21-1<3.5 g/L, CA125<35 U/mL, CA199<37 U/mL, AFP<20 ng/mL. More than the Normal reference value was judged as positive expression, when combined detection was performed, any positive expression was judged as overall positive expression.

2.4. Statistical Treatment

SPSS 19.0 was adopted for statistic analysis, (Mean ± SD) was used for quantitative data expression, variance analysis was used for comparison among groups, LSD test was used for comparison between any two means, χ² test was used for qualitative data comparison. Detection standard: α =0.05.

3. Results

3.1. Detection results of tumor markers in each group

CEA, NSE, CYFRA21-1, CA125, CA199 and AFP in A group was (17.56±8.38) g/L, (40.12±5.22) ng/mL, (7.32±2.41) μ g/L, (53.27±10.26) U/mL, (41.26±9.41) U/mL and (24.17±9.46) ng/mL respectively, which was significantly higher than that in B group and C group, and difference had statistical significance (P<0.05); comparative difference of tumor marker levels between B group and C group had no statistical significance (P>0.05). As was shown in Table 1.

3.2. Tumor marker levels of patients with different pathological types in A group

CEA and CYFRA21-1 of small cell lung cancer patients in A group was (26.32±9.16) g/L and (11.47±2.18) μ g/L respectively, which was significantly higher than that (3.21±1.6) g/L and (3.05±2.67) μ g/L of non-small cell lung cancer patients, however, NSE was(15.17±5.91) ng/mL, which was lower than that (43.18±8.82) ng/mL of non-small cell lung cancer patients, difference had statistical significance (P<0.05); CA125, CA199 and AFP comparative difference between small cell lung cancer patients and non-small cell lung cancer patients had no statistical significance (P>0.05). As was shown in Table 2.

Table 1.

Detection results of tumor markers in each group.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>CEA (g/L)</th>
<th>NSE (ng/mL)</th>
<th>CYFRA21-1 (μ g/L)</th>
<th>CA125 (U/mL)</th>
<th>CA199 (U/mL)</th>
<th>AFP (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>52</td>
<td>17.56±8.38</td>
<td>40.12±5.22</td>
<td>7.32±2.41</td>
<td>53.27±10.26</td>
<td>41.26±9.41</td>
<td>24.17±9.46</td>
</tr>
<tr>
<td>B</td>
<td>76</td>
<td>1.09±0.45</td>
<td>11.07±3.01</td>
<td>1.21±0.73</td>
<td>10.13±2.17</td>
<td>9.02±2.69</td>
<td>14.12±6.54</td>
</tr>
<tr>
<td>C</td>
<td>118</td>
<td>0.97±0.56</td>
<td>10.92±2.61</td>
<td>1.16±0.68</td>
<td>9.87±3.36</td>
<td>8.68±1.73</td>
<td>13.91±9.15</td>
</tr>
<tr>
<td>F</td>
<td>23</td>
<td>23.477</td>
<td>5.0625</td>
<td>30.629</td>
<td>45.321</td>
<td>40.369</td>
<td>10.667</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Notes: A and B group comparison, P<0.05; B and C group comparison, P<0.05.

Table 2.

Tumor marker levels of patients with different pathological types in A group.

<table>
<thead>
<tr>
<th>Types</th>
<th>n</th>
<th>CEA (g/L)</th>
<th>NSE (ng/mL)</th>
<th>CYFRA21-1 (μ g/L)</th>
<th>CA125 (U/mL)</th>
<th>CA199 (U/mL)</th>
<th>AFP (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small cell lung cancer</td>
<td>23</td>
<td>3.21±1.16</td>
<td>43.18±8.82</td>
<td>3.05±2.67</td>
<td>54.08±15.17</td>
<td>41.07±10.46</td>
<td>23.98±14.27</td>
</tr>
<tr>
<td>F</td>
<td>43.976</td>
<td>37.898</td>
<td>56.851</td>
<td>0.037</td>
<td>0.001</td>
<td>0.005</td>
<td>0.005</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>
3.3. Combined detection values of tumor markers

In separate tumor marker detection of lung cancer, sensitivity of CEA was the highest (50.00%), specificity of CA199 was the highest (91.24%). Sensitivity of combined detection of 6 tumor markers was 71.15%, and specificity was 89.69%. As was shown in Table 3.

Table 3. Combined detection values of tumor markers.

<table>
<thead>
<tr>
<th>Tumor Markers</th>
<th>Sensitivity(%)</th>
<th>Specificity(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CEA</td>
<td>50.00(26/52)</td>
<td>84.54(164/194)</td>
</tr>
<tr>
<td>NSE</td>
<td>44.23(23/52)</td>
<td>88.14(171/194)</td>
</tr>
<tr>
<td>CYFRA21-1</td>
<td>46.15(24/52)</td>
<td>90.72(176/194)</td>
</tr>
<tr>
<td>CA125</td>
<td>25.00(13/52)</td>
<td>87.11(169/194)</td>
</tr>
<tr>
<td>CA199</td>
<td>40.38(21/52)</td>
<td>91.24(177/194)</td>
</tr>
<tr>
<td>AFP</td>
<td>17.31(9/52)</td>
<td>84.54(164/194)</td>
</tr>
<tr>
<td>Combined Detection</td>
<td>71.15(37/52)</td>
<td>89.69(174/194)</td>
</tr>
</tbody>
</table>

4. Conclusion

In recent years, along with the increasing number of aging population in our country, pulmonary tuberculosis complicating lung cancer patients were significantly increasing accordingly. As was thought by Wang X[5] after reports on 278 clinical cases had been performed that once pulmonary tuberculosis complicating lung cancer could be early diagnosed, their five-year survival rate could be increased from 45%-55% to about 70%. In recent years, basic scientific researches on tumor markers largely promoted the application of serum tumor markers to early diagnosis of malignant tumors. Majority of scholars thought that CA125, CA199, AFP levels of peripheral blood of pulmonary tuberculosis complicating lung cancer patients were significantly increased. Meanwhile, after retrospective analysis of 1230 cases of Asian patients with lung cancer, Ghosh I[6] found that NSE, CYFRA21-1 levels were significantly increased among about 75%-80% of lung cancer patients, meanwhile, subgroup analysis results indicated that NSE and CYFRA21-1 were in significant correlation with illness state of pulmonary tuberculosis complicating lung cancer patients. As was thought by Zeng Y[7] that NSE and CYFRA21-1 combined with other tumor serological indicators could significantly promote the diagnosis levels of early stage clinical positive expression of pulmonary tuberculosis complicating lung cancer patients, and its sensitivity and specificity were higher.

CA125, as malignant tumor–related carbohydrate antigen, was at the earliest obtained in ovarian cancer cystadenoma cells through cross immunization with spleen cells of mice by WOOLS, and now was widely applied to early screening of ovarian cancer. Majority of scholars found that CA19-09 had obviously higher expression in the early stage of lung cancer tissues, meanwhile Zhiyun Ma thought that CA125 could be taken as the auxiliary reference indicator of clinical staging of lung cancer[8,9]. CA19-9, as other kind of carbohydrate antigen, was at the earliest found having obvious expression in peripheral blood of patients with gastrointestinal epithelial tumor cells; especially in liver tumors and bile duct epithelial cell tumors, CA19-9 expression was abnormally increased. CA19-9 could be accessible to blood through ductus thoracicus, and then increased the related markers levels of peripheral blood; CEA and AFP, as human embryo specific antigen related tumor markers, were found being increased obviously in peripheral blood of early-stage colon cancer patients; in addition, CEA and AFP were considered as having better specificity for the early diagnosis of gastrointestinal adenocarcinoma, however, in recent years, many scholars thought that CEA and AFP expression had no specificity, and they had obvious expression in peripheral blood of lung cancer patients, and they had important values for the early-stage diagnosis of stomach cancer[10]; NSE, as a kind of enolase involving in glycolytic pathway, existed in nerve and neuroendocrine tissues, was at the earliest found in tumours related with neuroendocrine tissue origin; however, in recent years, retrospective analysis and results of a large number of basic researches indicated that specific tumor markers of NSE lung cancer and neuroblastoma in children, CYFRA21-1 mainly existed in cytoplasm of lung cancer tumor cells, once tumor cell apoptosis occurred, CYFRA21-1 would be released to peripheral blood, thereby, which was considered as the up-regulation of related tumor markers[11].

In this study, 52 cases with pulmonary tuberculosis complicating lung cancer who were admitted in our hospital between January 2014 and April 2015 were selected and 76 cases with pulmonary tuberculosis were selected, and 118 cases with physical examination during the corresponding period were selected; and through CEA, NSE, CYFRA21-1, CA125, CA199 and AFP detection of related peripheral blood was performed, we found that CEA, NSE, CYFRA21-1, CA125, CA199 and AFP levels of peripheral blood of pulmonary tuberculosis complicating lung cancer patients were significantly higher than that of pulmonary tuberculosis patients and healthy cases, which indicated the possibility of CEA, NSE, CYFRA21-1, CA125, CA199 and AFP combined detection in the early screening of pulmonary tuberculosis complicating lung cancer. However, Mou W[11] found that CA125 expression in patients with pulmonary tuberculosis was obviously higher than that in healthy people; in addition, CA125 positive expression level in parts of patients with pulmonary tuberculosis complicating lung cancer was less than 70%, which indicated that CA125 expression had a certain non-specificity; after further analysis of subtype lung cancer pathology, we found that CEA and CYFRA21-1 expression in peripheral blood of small cell lung cancer patients were significantly increased, which was in accordance with the research results by Mou W[11], that was, due to poor cell differentiation, high atypia and easy invasion occurrence of small cell lung cancer patients, PI3K/AKT signal pathway on the surface of peripheral glands of small cell lung cancer was activated abnormally, cell cycle control was abnormal, CEA secretion was increased, in the meantime, along with the active proliferation of small cell lung cancer, blood supply was relatively insufficient, total apoptosis cells were increased, and released CYFRA21-1 was significantly increased[6,12]; however, through researches on NSE we found that its expression level was significantly decreased; as was thought by Zeng Y[7] that the significant decrease of NSE expression in small cell lung cancer patients was related with Notch signal pathway which was activated abnormally in partial small cell cancer, but related deep researches were not available.
Separate detection results analysis of 6 tumor markers indicated that sensitivity of 6 tumor markers was lower (CEA was the highest 50%), in the meanwhile, although their corresponding specificity was higher, they merged sensitivity in varying degrees; however, sensitivity of combined detection of 6 tumor markers was 71.15%, and specificity was 89.69%; on the basis of that specificity was not changed basically, sensitivity was significantly increased, which indicated the important values of combined detection in the early screening of pulmonary tuberculosis complicating lung cancer patients.

It followed that CEA, NSE, CYFRA21-1, CA125, CA199 and AFP had obvious expression in peripheral blood of pulmonary tuberculosis complicating lung cancer patients. Combined detection of 6 serum tumor markers could improve the lower sensitivity of separate serum tumor marker detection, and reduce the occurrence of false-negative cases in the early screening, which was deserved extensive clinical application.

References


