Value of serum tumor markers and cytokines detection in elderly patients with breast cancer

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ABSTRACT

Objective: To study the value of serum tumor markers CA125, CA153, CEA, -hCG, CA199, CYFRA21-1, beta and TPS cytokines IL-6, TNF- alpha, IL-8 and GDF-3 levels in the diagnosis of breast cancer, and provide reference for clinical diagnosis and treatment. Methods: A total of 293 cases of breast cancer patients admitted to our hospital from November 2015 to November 2017 were selected as the observation group. Besides, 125 patients with benign breast disease and 125 healthy people who came to our hospital for physical examination were also selected as benign breast disease group and control group, respectively. Serum tumor markers and cytokine changes were detected by using multiple tumor markers protein chip detection system and enzyme-linked immunosorbent assay (ELISA) among three groups. Results: Serum tumor markers and cytokine levels of observation group were higher than those in control group and benign breast disease group, the differences were statistically significant; through comparing different groups at different breast disease stages, serum tumor markers increase with the elevated stage, the highest in stage IV breast cancer. The difference was statistically significant; When benign breast disease group was compared with the control group, there was no significant difference in each index. Conclusion: The serum tumor markers CA125, CA153, CEA, -hCG, CA199, CYFRA21-1, beta and TPS cytokines IL-6, TNF- alpha, IL-8, GDF-3 show higher expression level in breast cancer and increase with the elevated stage. Therefore, it is worthy of attention.

1. Introduction

As one of the most common malignant tumors in clinical women, the incidence of breast cancer has gradually increased in recent years, and it has become the highest incidence of malignant tumor in China[1]. At present, the major means adopted clinically in the diagnosis of breast cancer are histopathological inventory analysis, scanning (positron emission tomography, PET), computed tomography (CT) scan and molybdenum target shooting etc. But the early diagnosis of breast density or the less tumor in patients with breast cancer is difficult[2]. According to the literature, there are 1.3 million new cases of breast cancer worldwide each year, of which there are about 470 000 deaths from breast cancer. Therefore, detection, diagnosis and treatment at the early stage is very important for patients with breast cancer. Studying tumor markers with high specificity and sensitivity contributes to early detection and diagnosis of breast cancer, and it has become a hot spot and focus on clinical research[3]. Therefore, we study the value of serum tumor markers CA125, CA153, CEA and beta hCG, CA199, CYFRA21-1, TPS and cytokine IL-6, TNF alpha, IL-8, GDF-3 level in diagnosis of breast cancer, which provides reference for clinical diagnosis and treatment.

2. Materials and methods

2.1 General information

A total of 293 cases of breast cancer patients admitted to our
hospital from November 2015 to November 2017 were selected as observation group, while 125 patients with benign breast disease and 125 healthy people who received physical examination were also selected as benign breast disease group and control group, respectively. There are 169 cases at stage I and II of breast cancer, 83 cases at stage III, and 91 cases at stage IV, aged 30 - 68, with average age (46±7). All patients with breast cancer were confirmed by cytology or pathological histology and signed a consent form. This study has been approved by the hospital ethics committee. All subjects were excluded from the chronic medical history of hypertension, diabetes and other internal medicine. The liver, kidney and heart function were normal, and no abnormalities were observed in chest or X-ray examination. The three groups of subjects were compared in terms of age and basic condition, and the difference was not statistically significant (P>0.05).

2.2 Diagnostic methods

All subjects were dawn peripheral venous blood 5 mL, on an empty stomach. The serum was separated under the following condition: centrifugal radius 15 cm, the speed of 2 500 r/min, the centrifugal time 10-12 min, and placed under -20 ℃ for further use. Serum CA125, CA153, CEA and beta hCG, CA199, CYFRA21-1, TPS were detected using C12 multiple tumor markers protein chip diagnostic kits and multiple tumor markers protein chip detection system (huzhou kang biological technology co., LTD.); Cytokine IL-6, TNF- alpha, IL-8 and GDF-3 were measured by ELISA assay (Gengyre). The test was conducted strictly according to the instructions of the kit.

2.3 Statistical methods

Count data and measurement data were analyzed in this study by using SPSS13.0 statistics analysis, P < 0.05 was demonstrated as statistically significant. Count data were expressed as the percentage in chi-square test; the measurement data were expressed as mean ± SD in t test. Pearson analysis was used for correlation analysis.

### Table 1

Comparison of serum cytokine index changes among the three groups (pg/mL).

<table>
<thead>
<tr>
<th>Groups</th>
<th>IL-6</th>
<th>IL-8</th>
<th>GDF3</th>
<th>TNF-α</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I and stage II breast cancer group</td>
<td>35.6±13.5</td>
<td>48.9±10.1</td>
<td>120.7±14.6</td>
<td>63.3±11.1</td>
</tr>
<tr>
<td>Stage III breast cancer group</td>
<td>48.6±14.6</td>
<td>69.6±11.2</td>
<td>135.1±21.1</td>
<td>79.8±12.5</td>
</tr>
<tr>
<td>Stage IV breast cancer group</td>
<td>59.6±15.2</td>
<td>115.5±19.6</td>
<td>158.9±28.6</td>
<td>87.5±15.9</td>
</tr>
<tr>
<td>Benign breast disease group</td>
<td>7.5±1.4</td>
<td>26.6±5.0</td>
<td>84.6±9.4</td>
<td>6.0±1.3</td>
</tr>
<tr>
<td>Control group</td>
<td>6.3±1.2</td>
<td>25.6±3.3</td>
<td>81.6±8.7</td>
<td>5.8±1.1</td>
</tr>
</tbody>
</table>

### Table 2

Comparison of serum tumor markers in the three groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>CA125 (μ/mL)</th>
<th>CA153 (μ/mL)</th>
<th>CA199 (μ/mL)</th>
<th>CEA (g/L)</th>
<th>β-hCG (g/L)</th>
<th>CYFRA21-1 (ng/mL)</th>
<th>TPS (μ/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I and stage II breast cancer group</td>
<td>48.6±11.6</td>
<td>38.5±10.5</td>
<td>36.7±10.6</td>
<td>7.5±1.3</td>
<td>6.8±1.6</td>
<td>38.5±7.5</td>
<td>22.6±8.5</td>
</tr>
<tr>
<td>Stage III breast cancer group</td>
<td>99.5±15.8</td>
<td>69.7±15.6</td>
<td>59.5±11.6</td>
<td>18.3±2.6</td>
<td>13.0±2.8</td>
<td>49.7±9.5</td>
<td>32.6±11.3</td>
</tr>
<tr>
<td>Stage IV breast cancer group</td>
<td>136.5±25.6</td>
<td>102.4±19.4</td>
<td>94.6±10.4</td>
<td>25.8±4.8</td>
<td>19.9±3.5</td>
<td>58.4±12.6</td>
<td>45.6±15.1</td>
</tr>
<tr>
<td>Benign breast disease group</td>
<td>17.1±1.4</td>
<td>9.4±1.3</td>
<td>10.5±3.9</td>
<td>2.3±0.7</td>
<td>2.4±0.5</td>
<td>12.5±3.8</td>
<td>7.6±1.2</td>
</tr>
<tr>
<td>Control group</td>
<td>14.5±1.2</td>
<td>7.5±1.0</td>
<td>7.2±3.5</td>
<td>1.5±0.3</td>
<td>1.3±0.2</td>
<td>11.9±3.1</td>
<td>6.3±0.9</td>
</tr>
</tbody>
</table>

3. Results

3.1 Comparison of serum cytokine index changes among the three groups

The levels of cytokines in different stages of breast cancer were higher than those in the control group and the benign breast disease group, and the differences were statistically significant (P<0.05). Compared with different stages of breast cancer, the serum cytokines increased with the increase of stages, with the highest at stage IV, and the difference was statistically significant (P<0.05). There was no statistically significant difference between the benign breast disease group and the control group (P>0.05) (Table 1).

3.2 Comparison of serum tumor markers in the three groups

The levels of serum tumor markers in different stages of breast cancer were higher than those in the control group and the benign breast disease group, and the differences were statistically significant (P<0.05). Comparison between groups of different stages of breast cancer, the serum tumor markers elevated with the elevated stage, the highest at IV stage of breast cancer. The difference was statistically significant (P < 0.05); There was no statistically significant difference between the benign breast disease group and the control group (P>0.05) (Table 2).

4. Discussion

As one of the most common malignant tumors in clinical gynecological treatment, the early stage of breast cancer does not have typical signs and symptoms, and misdiagnosis[4]. Recent statistics have found that the incidence of breast cancer in China shows a trend towards younger age, and the incidence of breast cancer is increasing, which brings about greater physical and mental pressure[5]. At present, the diagnosis of breast cancer is mainly
based on history and physical examination, along with imaging examination. The combination of breast ultrasound and X-ray has become a common screening means for breast cancer, but the diagnosis of breast cancer is mainly dependent on histopathological examination[6]. Tumor cell secretion or a small amount of active substance in tissue or fluid is called tumor markers, including CA125 and CA153 which have been widely used in the diagnosis and treatment of breast cancer[7]. Therefore, it is very important how to combine serum tumor markers CA125, CA153, CEA, beta-hcg, CA199, cyfra21-1, TPS, and cytokine il-6, tnf-alpha, il-8, and gdf-3 to diagnose breast cancer and its progress[8].

The levels of serum tumor markers in different stages of breast cancer in each group were higher than those in the control group and the benign breast disease group, and the differences were statistically significant (P<0.05). Compared with different stages of breast cancer, with the increase of stage, the serum tumor markers were all elevated, with the highest at stage IV. The difference was statistically significant (P<0.05). There was no statistically significant difference between the benign breast disease group and the control group (P>0.05). In recent years, the reports on CA125, CA153 and CA199 are relatively high, which have a higher specificity for breast cancer diagnosis, but the positive rate is lower[9]. As an important monitoring marker for invasive or metastatic breast cancer, early sensitivity of CA153 is also poor, so it is necessary to combine other indicators to diagnose the disease[10]. As a non-specific tumor marker, CEA will increase in different degrees in adenocarcinoma such as gastric cancer and breast cancer[11]. In addition, CEA can be used to evaluate the prognosis of breast cancer patients. The levels of cytokines in different stages of breast cancer were higher than those in the control group and the benign breast disease group, and the differences were statistically significant (P<0.05). Compared with different stages of breast cancer, the serum cytokines increased with the increase of stages, the highest at stage IV. The difference was statistically significant (P<0.05). There was no statistically significant difference between the benign breast disease group and the control group (P>0.05). Studies suggest that tumor, T and B lymphocytes or fiber cells can produce IL-6, it can produce two kinds of expressions, one produced in the stimulation induced, the other expressed under the state of nature[12]. It is also found that the occurrence and development of bone tumors are positively correlated with the increase of IL-6 level in serum. Other studies suggest that IL-8 can be released by tumor cells and related macrophages[13]. Based on the results of this study, it isreasonable to believe that the increase of IL-6 level in serum is positively correlated with tumor progression. As one of the strongest anti-tumor cytokines, TNF-alpha is a soluble and multi-active protein cytokine induced by monocyte macrophages[14]. Currently, it is widely believed that TNF-alpha has a significant anti-tumor effect outside the body, which can interact with other cytokines to produce synergistic effect on the growth and differentiation of tumor cells. Some studies have suggested that the higher the TNF-alpha level in breast cancer patients is, the higher the metastasis and recurrence rate is, which can serve as an important reference indicator for determining the progress of the disease and its possible metastasis[15].

In a nutshell, serum tumor markers CA125, CA153, CEA and beta hCG, CA199, CYFRA21-1, TPS and cytokine IL-6, TNF-alpha, IL-8, GDF-3 show higher expression in breast cancer, and rise at any stage, which is worthy of clinical attention.

References