Clinical significance of serum tumor markers and cytokines in the detection of breast cancer

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Objective: To explore the clinical significance of serum tumor markers and cytokines in the detection of breast cancer. Methods: A total of 586 different breast cancer staging, 250 patients with benign breast disease and 250 controls were detected and compared the serum tumor markers (CA125, CA153, CA199, CEA, β-hCG, CYFRA21-1, TPS) and cytokines (TNF-α, IL-6, IL-8, GDF3) level. Results: The serum tumor staging of breast cancer were different markers (CA125, CA153, CA199, CEA, β-hCG, CYFRA21-1, TPS) and cytokines (TNF-α, IL-6, IL-8, GDF3) were higher than those in control group and benign breast disease group and had statistical difference, serum tumor between different groups of breast cancer staging markers and cytokine levels were statistically different, with the staging of elevated serum tumor markers were increased with stage IV breast cancer group was the highest, was found between the control group and the benign breast disease group serum tumor marker was found the difference and cytokine. Conclusion: Serum tumor markers (CA125, CA153, CA199, CEA, β-hCG, CYFRA21-1, TPS) and cytokines (TNF-α, IL-6, IL-8, GDF3) in breast cancer detection have important clinical significance.

1. Introduction

Breast cancer is a relatively common malignant tumor in recent years. With the advancement of medical technology, the mortality rate of breast cancer is decreasing year by year, but its incidence is increasing year by year, and the age of onset is younger[1,2]. If the breast cancer early detection, early diagnosis and early treatment can significantly reduce the mortality of patients, improve the cure rate, improve the quality of life and reduce the burden of disease, and most of the early breast cancer did not have clinical symptoms, so to find the early detection of breast cancer blood indicators for the occurrence, development, treatment and prognosis of breast cancer has important clinical significance[3]. In this study, we studied the changes of serum tumor markers and cytokines in patients with breast cancer, and to explore its clinical value in the detection of breast cancer, and to provide theoretical basis for early diagnosis of breast cancer.

2 Data and methods

2.1 Clinical data

A total of 586 cases of patients with breast cancer from January 2015 to September 2016 in the breast surgery of our hospital for treatment were selected as the research subject, women, divided into three groups according to the staging of breast cancer[4], including 75 cases of stage I, 162 cases of stage II, as stage I and II breast cancer group, the average age 49; 166 cases in stage III, as stage III breast cancer group, the average age 48; 183 cases as stage IV breast cancer group, the average age 52 years old. Inclusion criteria: 1) Patients with breast cancer were diagnosed by pathological examination; 2) breast cancer diagnostic criteria in reference to the relevant standards of the 2013 China Anti-Cancer Association, "the Chinese Association for the treatment of breast cancer guidelines
and guidelines for the treatment of breast cancer[4]; 3) blood samples were collected before surgery, chemotherapy, radiotherapy and drug treatment; 4) medical history data integrity. Exclusion criteria: 1) patients with severe infection, heart, liver and kidney dysfunction, metabolic diseases; 2) patients with a history of other malignancies; 3) patients with pregnancy and lactation. 250 patients with benign breast disease who were hospitalized in the breast surgery of our hospital were selected as benign breast disease group, female, the average age 45 years old, including 122 cases of breast fibroadenoma, 60 cases of breast adenosis, 68 cases of breast cystic hyperplasia, inclusion criteria: 1) benign breast disease patients were diagnosed by histopathological examination; 2) past and hospital examination were not found in malignant tumors; 3) before the blood samples were not received drug treatment; 4) Medical history data integrity. Exclusion criteria were same with breast cancer. Then select 250 cases of women breast disease patients of our hospital at the same period from the physical examination center as the control group, the average age 47 years old, were not infected, heart, liver and kidney dysfunction, with metabolic diseases and breast disease, non-pregnancy and lactation. There was no statistically significant difference between breast cancer patients in stage I, II, III and stage IV, benign breast disease and control group (P>0.05).

2.2 Sample collection and laboratory examination

5 mL fasting venous blood samples were collected from all the subjects in the morning, serum was separated and serum tumor markers, isolated serum, detect the serum tumor markers: serum carbohydrate antigen 125 (carbohydrate antigen 125, CA125), serum carbohydrate antigen 153 (carbohydrate antigen 153, CA153), serum carbohydrate antigen 199 (carbohydrate antigen 199, CA199), carcinoembryonic antigen (cancer embryo antigen, CEA), human chorionic gonadotropin (human chorionic gonadotropin, hCG), cytokeratin 19 fragment antigen 21-1 (cytokeratin 19 fragment antigen 21-1, CYFRA21-1) and tissue polypeptide specific antigen (tissue polypeptide-specific antigen, TPS) and cytokines: tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), interleukin-8 (IL-8), human growth differentiation factor 3 (GDF3), including CA125, CA153, CA199, CEA, β-hCG, CYFRA21-1, TPS beta with multiple tumor marker protein chip detection system (C12) testing (Shanghai healthdigit Co.), TNF-α, IL-6, IL-8 and GDF3 were detected by enzyme linked immunosorbent assay kit. According to the Shanghai co-side box for the company’s production, testing in strict accordance with the instructions.

2.3 Statistical analysis

Epi Data 3.0 software was used to record the data, and SPSS 19.0 software package was used for statistical analysis. The measurement data were expressed as mean ± standard deviation (Mean ± SD), and the comparison was analyzed by ANOVA. The SNK method was used to compare between two groups, and P<0.05 was considered statistically significant.

3. Results

3.1 Comparison of serum tumor marker levels in five groups subjects

There were significant differences in serum tumor markers (CA125, CA153, CA199, CEA, β-hCG, CYFRA21-1, TPS) among the five groups (P<0.05), the serum tumor markers levels at different breast cancer staging (CA125, CA153, CA199, CEA, β-hCG, CYFRA21-1, TPS) were significantly higher than those of the control group and benign breast disease group (P<0.05). There were significant differences in serum tumor markers (CA125, CA153, CA199, CEA, β-hCG, CYFRA21-1, TPS) at different stages of breast cancer between the groups (P<0.05). With the increase of stage, the serum tumor markers were elevated, the stage IV breast cancer group was the highest, no significant difference was found in serum tumor markers (CA125, CA153, CA199, CEA, β-hCG, TPS).

Table 1. Comparison of serum tumor marker levels in five groups subjects.

<table>
<thead>
<tr>
<th>Tumor markers</th>
<th>Control group (n=250)</th>
<th>Benign breast disease group (n=250)</th>
<th>I stage, II stage breast cancer group (n=237)</th>
<th>III stage breast cancer group (n=166)</th>
<th>IV stage breast cancer group (n=183)</th>
<th>F value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA125 (U/mL)</td>
<td>13.35±2.55</td>
<td>17.10±10.44</td>
<td>48.58±21.65*</td>
<td>99.46±35.82*</td>
<td>136.48±45.66*</td>
<td>867.472</td>
<td>0.000</td>
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<tr>
<td>CA153 (U/mL)</td>
<td>7.48±2.01</td>
<td>9.45±4±26</td>
<td>38.54±20.48*</td>
<td>69.66±25.57*</td>
<td>102.37±39.43*</td>
<td>740.053</td>
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<tr>
<td>CA199 (U/mL)</td>
<td>7.20±4.52</td>
<td>10.51±3.94</td>
<td>35.65±14.58*</td>
<td>59.48±21.55*</td>
<td>94.55±40.35*</td>
<td>680.427</td>
<td>0.000</td>
</tr>
<tr>
<td>CEA (g/L)</td>
<td>1.49±1.03</td>
<td>2.25±1.27</td>
<td>7.45±2.25*</td>
<td>18.28±9.62*</td>
<td>25.82±12.88*</td>
<td>511.144</td>
<td>0.000</td>
</tr>
<tr>
<td>ß-hCG (g/L)</td>
<td>1.12±1.00</td>
<td>1.59±1.24</td>
<td>6.78±3.57*</td>
<td>12.95±5.78*</td>
<td>19.98±7.45*</td>
<td>739.259</td>
<td>0.000</td>
</tr>
<tr>
<td>CYFRA21-1 (ng/mL)</td>
<td>11.58±5.45</td>
<td>12.49±6.81</td>
<td>38.52±7.49*</td>
<td>49.65±9.48*</td>
<td>58.77±12.57*</td>
<td>1 398.158</td>
<td>0.000</td>
</tr>
<tr>
<td>TPS (U/L)</td>
<td>6.25±1.38</td>
<td>7.57±1.67</td>
<td>22.55±8.54*</td>
<td>32.64±11.35*</td>
<td>45.59±15.42*</td>
<td>759.924</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Compared with the control group,*P<0.05; compared with benign breast disease group, **P<0.05; with stage I and II breast cancer group, ***P<0.05; compared with stage III breast cancer group, ****P<0.05.
3.2 Comparison of cytokines in five groups of subjects

Cytokines (TNF-α, IL-6, IL-8, GDF3) of the five groups were statistically different \((P<0.05)\), the cytokinesin different stage of breast cancer groups (TNF-α, IL-6, IL-8, GDF3) were higher than those in control group and benign breast disease group and there were statistical differences (all \(P<0.05\)),there was statistical difference in cytokines (TNF-α, IL-6, IL-8, GDF3) between different stages of the breast cancer group \((P<0.05)\). With the increase of stage, the cytokines (TNF-α, IL-6, IL-8, GDF3) all increased, and stage | breast cancer group was the highest, no statistically significant differences were found in cytokines (TNF-α, IL-6, IL-8, GDF3) between the control group and the benign breast disease group (all \(P>0.05\)). See table 1.

4. Discussion

With the rapid development of immunolabeling technology, more and more tumor markers can be detected, which play an increasingly important role in tumor diagnosis, curative effect observation and prognosis.[5] Through the study of the changes of serum tumor markers (CA125, CA153, CA199, CEA, β-hCG, CYFRA21-1, TPS) and cytokines (TNF-α, IL-6, IL-8, GDF3) in breast cancer patients to provide a theoretical basis on early diagnosis.

CA125 is a carbohydrate antigen, which in breast cancer, especially ovarian cancer has an important diagnostic value, not only can determine the disease progression, but also act as an important prognostic indicators;[6] CA153 is also a carbohydrate antigen, which has important relevance with the breast cancer, ovarian cancer and endometrial cancer, but also has important clinical value in judging the progress of disease[7,8]; CA199 is a mucin type carbohydrate protein tumor marker, a sugar lipid on cell membrane, molecular weight greater than 1 000 kD, it is in the form of salivary mucin in the serum, located in the normal fetal pancreas, gallbladder, liver, intestine and normal adult pancreas, bile duct epithelium, an associated antigen present in the blood circulation of gastrointestinal cancer[9,10]; CEA has an important diagnostic value on gynecological malignancies, breast cancer, lung cancer, liver cancer and other digestive system malignant tumors[11,12]; β-hCG is a glycoprotein hormone, have important diagnosis value on breast cancer and gynecological tumors[13-15]; CYFRA21-1, no expression or low expression under normal conditions, is found to be highly expressed in breast cancer, but its level is reduced to normal after surgery[16]; TPS is epithelial cell-derived malignancies and highly expressed in the metastatic cancer, is an important tumor marker[17].

There were significant differences in serum tumor markers (CA125, CA153, CA199, CEA, β-hCG, CYFRA21-1, TPS) among the five groups (CA125, CA153, CA199, CEA, β-hCG, CYFRA21-1, TPS) \((P<0.05)\), and the different tumor markers (CA125, CA153, CA199, CEA, β-hCG, CYFRA21-1, TPS) among the breast cancer groups in different stages were significantly higher than those in the control group and benign breast disease group (all \(P<0.05\)), and were all statistically different \((P<0.05)\), and the different tumor markers (CA125, CA153, CA199, CEA, β-hCG, CYFRA21-1, TPS) in different stages among the breast cancer groups were all statistically different \((P<0.05)\), with the increase of the tumor stage, the serum tumor markers all increased; the stage | breast cancer group was the highest, no significant differences was found in serum tumor markers (CA125, CA153, CA199, CEA, β-hCG, CYFRA21-1, TPS) between the control group and benign breast disease group (mean \(P>0.05\)). It suggested that CA125, CA153, CA199, CEA, beta-hCG, CYFRA21-1 and TPS have important clinical significance in the diagnosis of breast cancer, and increase with the clinical stage of breast cancer.

TNF-α is an important anti-tumor cytokine, which reflects the level of high metastasis and recurrence of malignant tumors[18]; The rise of IL-6, IL-8 levels in malignant tumor has a positive correlation with tumor progression[19,20]; GDF3 is also an important tumor-

<table>
<thead>
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</tr>
<tr>
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<td>CYFRA21-1 (ng/mL)</td>
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<tr>
<td>TPS (U/L)</td>
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</table>

Compared with the control group, *\(P<0.05\); compared with benign breast disease group, †\(P<0.05\); with stage | and || breast cancer group, ★\(P<0.05\); compared with stage ||| breast cancer group, ★★\(P<0.05\).
releasing cytokines, has an important role in the occurrence of tumors[21]. The study found that the cytokines (TNF- α, IL-6, IL-8, GDF3) of the five groups were statistically different (P<0.05), the cytokines (TNF- α, IL-6, IL-8, GDF3) in different stage of breast cancer groups were higher than those in control group and benign breast disease group and there were statistically different (P<0.05), the comparison of the cytokines (TNF- α, IL-6, IL-8, GDF3) between different stages of the breast cancer group were statistically different (P<0.05), the cytokines (TNF- α, IL-6, IL-8, GDF3 alpha) increased with the staging, and the IV breast cancer group was the highest, no statistically significant difference was found in cytokines (TNF- α, IL-6, IL-8, GDF3) between control group and benign breast disease group (all P> 0.05). So TNF- α, IL-6, IL-8, GDF3 also has important clinical significance in the diagnosis of breast cancer, and increased with the clinical stage of breast cancer.

Routinely monitoring the serum tumor markers(CA125, CA153, CA199, CEA, β-hCG, CYFRA21-1, TPS) and cytokines (TNF- α, IL-6, IL-8, GDF3) in high-risk populations is helpful to the early diagnosis of breast cancer, and has important clinical significance for breast cancer staging and prognosis evaluation.

Reference


