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ABSTRACT

Objective: To study the serum tumor markers, immunoglobulin, TNF-α and hs-CRP in breast cancer in different pathological stages of the concentration, and to analyze the clinical significance of early diagnosis of breast cancer. Methods: A total of 130 patients with breast cancer were divided into stage I, II, III and IV according to clinical pathology. In addition, 40 patients with benign breast disease and 35 healthy subjects were selected as benign breast disease group and control group. Serum tumor markers, immunoglobulin, TNF-α and hs-CRP concentrations were measured and compared of all subjects. Results: There were no significant difference in serum tumor markers, immunoglobulin and inflammatory factors between the control group and the benign breast cancer group. The level of serum tumor markers in breast cancer group was significantly higher than that in control group and benign breast cancer group. The levels of serum CA125, CA153 and CEA were gradually increased with the severity enhancing from stage I and IV of breast cancer, and the difference was statistically significant. The level of serum immunoglobulin in breast cancer group was significantly higher than that in control group and benign breast cancer group. The levels of serum IgG and IgM increased gradually severity enhancing from stage I and IV of breast cancer, and the difference was statistically significant. The level of serum TNF-α and hs-CRP in serum of breast cancer group was significantly higher than that of control group and benign breast cancer group. The serum levels of TNF-α and hs-CRP increased gradually with severity enhancing from stage I and IV of breast cancer, and the difference was statistically significant. Conclusion: The level of serum tumor markers in breast cancer patients is increasing. Humoral and inflammatory responses are activated to varying degrees and increase with the aggregation of disease. They may involve regulating the occurrence and metastasis of breast cancer and regulating the pathophysiological function of patients. Which may be a certain clinical significance for the early diagnosis of breast cancer and disease progression.

1. Introduction

Breast cancer was common malignant tumor threatened mental and physical health of women, its occurrence rate gradually increases and becomes more and more younger[1,2]. Found and
2. Clinical material and method

2.1. Material

A total of 130 cases of patients with breast cancer (breast cancer group) admitted in our hospital from August 2015 to January 2017, 40 patients with benign breast disease (benign breast disease group) and 35 healthy subjects (control group) were selected. All of patients were female. Patients with breast cancer in stage I, II were 60 cases, aged from 43-68 years old; patients with breast cancer in stage III were 35 cases, aged from 45-70 years old; patients with breast cancer in stage IV were 35 cases, aged from 44-69 years old. Patients with benign breast disease were 41-68 years old, hyperplasia of mammary glands 16 cases, fibroadenoma of breast 20 cases, galactoma 4 cases. Normal examination was 40-67 years old. All of subjects’ genders, age were no statistical difference, it was comparable. Patient personally was informed and signed informed consent, this research was approved by ethics committee of hospital.

2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) all subjects were accorded with diagnostic criteria of breast cancer; (2) before extracted blood, the patients did not undergo any surgery and drug treatment; (3) completed clinical data. Exclusion criteria: (1) Subjects were with other malignant tumors; (2) subjects were with severe mental disease; (3) subjects were heart, pulmonary, renal dysfunction.

Inclusion criteria of benign breast disease: (1) subjects were diagnosed through pathological tissue examination; (2) subjects were with no history of malignant tumor; (3) subjects did not undergo any surgery and drug treatment; (4) completed clinical data. Exclusion criteria were same as the breast cancer.

2.3. Observation index

Extracted 3-4 mL of venous blood of patients, centrifuge and obtained supernatant for detection. Serum tumor markers indexes: serum carbohydrate antigen 125 (CA125), serum carbohydrate antigen 153 (CA153) and cracino-embryonic antigen (CEA) were respectively (112.44±41.57) U/mL, (87.63±27.18) U/mL and (21.43±15.61) μg/L, which was higher than stage I, II, III of breast cancer group at stage IV were respectively (81.73±33.54) U/mL, (57.81±21.75) U/mL and (13.65±7.28) μg/L, which was higher than stage I, II, III of breast cancer group, the difference was statistical (P<0.05); serum CA125, CA153 and CEA level in breast cancer group at stage IV were respectively (112.44±41.57) U/mL, (87.63±27.18) U/mL and (21.43±15.61) μg/L, which was higher than stage I, II, III of breast cancer group, the difference was statistical (P<0.05); serum CA125, CA153 and CEA level in breast cancer group at stage IV were respectively (112.44±41.57) U/mL, (87.63±27.18) U/mL and (21.43±15.61) μg/L, which was higher than stage I, II, III of breast cancer group, the difference was statistically significant (P<0.05). As shown in Table 1.

### Table 1.
Change of tumor markers level of patients in all groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>CA125 (U/mL)</th>
<th>CA153 (U/mL)</th>
<th>CEA (μg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>35</td>
<td>12.64±2.37</td>
<td>7.74±1.78</td>
<td>1.65±1.04</td>
</tr>
<tr>
<td>Benign breast disease group</td>
<td>40</td>
<td>16.35±7.14</td>
<td>9.03±2.43</td>
<td>2.37±1.36</td>
</tr>
<tr>
<td>Breast cancer group</td>
<td>130</td>
<td>75.63±27.54</td>
<td>51.43±19.75</td>
<td>11.55±6.73</td>
</tr>
<tr>
<td>Stage I, II</td>
<td>60</td>
<td>39.94±24.65</td>
<td>27.82±13.34</td>
<td>7.32±3.51</td>
</tr>
<tr>
<td>Stage III</td>
<td>35</td>
<td>81.73±33.54</td>
<td>57.81±21.75</td>
<td>13.65±7.28</td>
</tr>
<tr>
<td>Stage IV</td>
<td>35</td>
<td>112.44±41.57</td>
<td>87.63±27.18</td>
<td>21.43±15.61</td>
</tr>
</tbody>
</table>

Note: compared with control group, *P*<0.05; compared with benign breast disease, †*P*<0.05, compared with stage I, II of breast cancer group, ‡*P*<0.05, compared with stage III of breast cancer group, §*P*<0.05.
3.2. Comparison of serum immunoglobulin level in all groups

There was no obvious difference in serum IgA, IgG and IgM level of control group and benign breast disease ($P>0.05$), moreover serum IgA level of all groups was no obvious difference ($P>0.05$). Serum IgG and IgM level in different stage of breast cancer group (stage I, II, III, IV) were significantly higher than control group and benign breast disease group, the difference was significant ($P<0.05$); Serum IgG and IgM level of breast cancer at stage IV were $(16.63±3.58)$ g/L and $(1.73±0.46)$ g/L, which was higher than stage I, II, III of breast cancer group, the difference was statistical ($P<0.05$). As shown in Table 2.

Table 2.

Comparison of serum immunoglobulin level in all groups (g/L).

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>IgA</th>
<th>IgG</th>
<th>IgM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>35</td>
<td>0.72±0.27</td>
<td>7.14±2.38</td>
<td>0.58±0.24</td>
</tr>
<tr>
<td>Benign breast disease group</td>
<td>40</td>
<td>0.73±0.24</td>
<td>7.36±2.43</td>
<td>0.61±0.36</td>
</tr>
<tr>
<td>Breast cancer group</td>
<td>130</td>
<td>0.74±0.23</td>
<td>9.83±3.75</td>
<td>1.43±0.42</td>
</tr>
<tr>
<td>Stage I, II</td>
<td>60</td>
<td>0.72±0.25</td>
<td>8.82±3.34</td>
<td>1.21±0.51</td>
</tr>
<tr>
<td>Stage III</td>
<td>35</td>
<td>0.75±0.24</td>
<td>11.81±3.75</td>
<td>1.45±0.36</td>
</tr>
<tr>
<td>Stage IV</td>
<td>35</td>
<td>0.77±0.27</td>
<td>14.63±3.58</td>
<td>1.73±0.46</td>
</tr>
</tbody>
</table>

Note: compared with control group, $P<0.05$; compared with benign breast disease, $P<0.05$, compared with stage I, II of breast cancer group, $P<0.05$, compared with stage III of breast cancer group, $P<0.05$.

3.3. Comparison of serum TNF-α and hs-CRP level in all groups

There was no obvious difference in serum TNF-α and hs-CRP level in control group and benign breast disease group ($P>0.05$); Serum TNF-α and hs-CRP level at different stage of breast cancer group (stage I, II, III, IV) were significantly higher than control group and benign breast disease group, the difference was significant ($P<0.05$); Serum TNF-α and hs-CRP level of breast cancer at stage IV were $(106.44±14.87)$ pg/L and $(15.63±6.38)$ mg/L, which was higher than stage I, II, III of breast cancer group, the difference was statistical ($P<0.05$); Serum TNF-α and hs-CRP level of breast cancer at stage III were $(94.43±12.65)$ pg/L and $(11.65±5.83)$ mg/L, which was higher than stage I, II of breast cancer group, the difference was statistically significant ($P<0.05$). As shown in Table 3.

Table 3.

Comparison of serum TNF-α and hs-CRP level in all groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>TNF-α (pg/L)</th>
<th>hs-CRP (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>35</td>
<td>73.43±10.68</td>
<td>2.35±1.24</td>
</tr>
<tr>
<td>Benign breast disease group</td>
<td>40</td>
<td>75.01±10.97</td>
<td>2.67±1.36</td>
</tr>
<tr>
<td>Breast cancer group</td>
<td>130</td>
<td>96.43±12.67</td>
<td>11.65±5.83</td>
</tr>
<tr>
<td>Stage I, II</td>
<td>60</td>
<td>83.62±13.34</td>
<td>8.32±2.12</td>
</tr>
<tr>
<td>Stage III</td>
<td>35</td>
<td>94.43±15.56</td>
<td>12.71±5.75</td>
</tr>
<tr>
<td>Stage IV</td>
<td>35</td>
<td>106.44±14.87</td>
<td>15.63±6.38</td>
</tr>
</tbody>
</table>

Note: compared with control group, $P<0.05$; compared with benign breast disease, $P<0.05$, compared with stage I, II of breast cancer group, $P<0.05$, compared with stage III of breast cancer group, $P<0.05$.

4. Discussion

Breast cancer was a kind of high malignant tumor occurred in women, seriously affected healthy life of human[8]. Early clinical symptom was not obvious, therefore clinical early diagnosis and treatment was the research difficult problem and hot. At present, in addition to X-ray examination, ultrasound and immunohistochemistry, serum inspection was widely used in early diagnosis of breast cancer[9]. This paper was aimed to explore the significance of serum tumor markers, immunoglobulin, TNF-α and hs-CRP in early diagnosis of breast cancer in clinic.

Tumor markers referred to the substance that secreted by malignant tumor cell or generated by host cell by stimulating it in the process of tumor development, existed in the excreta, blood or tissue, it was the referred indexes for early diagnosis of tumor, evaluation of illness condition and monitor prognosis[10]. Tumor marker CA125, CA153 and CEA were closely related to breast cancer development. This research showed that: serum CA125, CA153 and CEA level in breast cancer group were significantly higher than control group and benign breast disease group, moreover along with stage I, II, III, IV increased, CA125, CA153 and CEA level were gradually enhanced. The reason might be that CEA was a broad-spectrum malignant tumor marker glycoprotein[11], CA125 was a carbohydrate antigen existed in body cavity epithelium of embryo development, both overexpressed in multiple tumors, usually used to diagnose illness condition and monitor the efficacy[12]. Along with breast cancer cells infiltration and transfer, serum CEA and CA125 level was gradually increased, they were good indexes that detected development of breast cancer. Whereas their specificity and sensitivity were common, usually combined with other markers to detect. CA153 was a transmembrane protein from breast epithelium, was critical marker in early diagnosis of breast cancer. CA153 could reduce the interaction between cancer cell, host cell and cellular matrix, inhibit lymphocyte factor and T cell activate and kill cell, promote breast cancer transfer and develop[13-15]. When breast cell became cancerization, activated glycosyl transferase caused carbohydrate antigen on the cell surface change and generate CA153, and due to cytoskeleton was destroyed, CA153 fell off from cancer cell and released to blood circulation, serum CA153 presented high expression[16]. CA153 was important marker detected breast cancer infiltration or transfer, along with tumor develop and transfer, serum CA153 gradually increased. However, specificity and sensitivity of CA153 in early clinical diagnosis was not excellent, presented negative expression in a part of patients. Therefore in clinic combined CA125 with CA153 and CEA, could enhance ate accuracy of early diagnosis and with certain value for evaluation of illness condition of breast cancer.

In addition, development of breast cancer was regulated by multiple immune factors, humoral immunity played defense function in patients with breast cancer, was the process of dissolved tumor cell that specific combination with antibody through activated complement system[17]. Immunoglobulin was a kind of antibody active molecule reflected humoral immunity. This research found that IgA level in all groups was not different, however, along with different stage of breast cancer (stage I, II, III, IV), serum IgG,
IgM level was gradually increased. The reason might be B cell function of patients with breast cancer was theneric, concentration of serum immunoglobulin was abnormal. IgA was a part of mucosa defence, not closely related to development of breast cancer, serum concentration was not changed. Whereas IgA was main serum immunoglobulin and was the most pivotal and most lasting antibody in the primary immune response. And IgG could promote phagocytosis of macrophage and play anti-infection effect. IgM was the earliest immunoglobulin in the primary immune response, in clinic mainly used to early diagnosis and infection[18]. Illness condition of breast cancer developed from stage I to IV, humoral immunity was enhanced gradually, serum IgG and IgM increased. Therefore, detected serum immunoglobulin level was important for early diagnosis and condition judgement.

Along with cancer cell infiltration and transfer, B cell was hyperfunction, inflammatory reaction was strong[19,20], TNF-α was biological active peptide secreted by macrophage, was the first cytokine used in cancer therapy[21], hs-CRP was a acute phase protein produced by liver cell, its serum concentration was positively relevant with degree of inflammatory reaction, in clinic widely applied to judge the course of multiple diseases[22]. Inflammatory factors TNF-α and hs-CRP over-expressed in breast cancer and other malignant diseases. This paper found that serum inflammatory factor in breast cancer group was obviously higher than control group and benign breast disease group, followed the stage I developed to stage IV in patients with breast cancer, serum TNF-α and hs-CRP level was gradually increased. The reason might be that abnormal immune function in patients with breast cancer could induce macrophage secrete massive TNF-α, thereby cause general inflammatory reaction, promote liver cell release acute phase protein, resulted in serum hs-CRP increasing[23]. research found that along with symptom becoming better, serum hs-CRP, TNF-α level was decreased[24]. Therefore, hs-CRP, TNF-α level was critical to evaluate breast cancer development and diagnostic condition.

In conclusion, different stage of breast cancer group (stage I, II, III, IV), serum tumor marker, immunoglobulin and inflammatory factor were increased at different degree. Tumor marker CA125, CA153 and CEA level change may involve in and regulate genesis and transfer of breast cancer, serum TNF-α, hs-CRP and immunoglobulin level might regulate pathological function of breast cancer. Combined detection was with certain value for early diagnosis of breast cancer.

Reference