<table>
<thead>
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<th>タイトル</th>
<th>高度癌の再発リスクを示す要因に関する研究</th>
</tr>
</thead>
<tbody>
<tr>
<td>著者</td>
<td>木田, 雅男; 龍部, 博洋; 川原, 勤一郎; 原, 守之助; 雅, 宏; 田渕, 弘幸; 萩原, 真明</td>
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<tr>
<td>発行日</td>
<td>1991-12-25</td>
</tr>
<tr>
<td>URL</td>
<td><a href="http://hdl.handle.net/10069/15895">http://hdl.handle.net/10069/15895</a></td>
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NAOSITE: 長崎大学学術研究成果リポジトリ
Risk Factor for Recurrence of Breast Cancer

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Received for publication, June 20, 1991

ABSTRACT: The risk factors of recurrence following surgical treatment for patients with breast cancer were clinically evaluated on the basis of a result of clinical analysis. In this study, it is emphasized that special attention should focus on tissue CEA and DNA analysis. In conclusion, clinical uses of tissue positive CEA and aneuploid pattern in analysis of nuclear DNA content in cancer cells are of great value to forecast recurrence.

INTRODUCTION

Progression of breast cancer completes a distant metastasis to the lung and the liver in 70% of patients and 50% of bone metastasis. As the symptoms are complex, so it is difficult to care for these patients.

In this study, the risk factors for recurrence of breast cancer was clinically assessed in the analysis of clinical experience with 43 patients with recurrence of breast cancer.

In fact, recurrence of breast cancer commonly occurred as being local and distant metastasis. It is well known that distant metastases are seen in the bone, the lung, the liver and the brain. On the other hand, local metastasis is composed of local recurrence of the thoracic wall and bulky node metastasis in the neighboring nodes.

The purpose of this study is to certify the risk factor for recurrence of breast cancer in the clinical analysis of 43 patients with recurrence and to prevent recurrence of breast cancer following surgery.

PATIENTS

Table 1 showed recurrent organs in patients with breast cancer. The most predominant sites were the lung and the skin, followed by the bone, the lymphnodes, the liver and the pleura.

It implies that the lung and the liver which receives a large amount of blood is a favorable site for recurrence. Recurrence of local skin should be avoided by meticulous surgical technique, which prevent tumor cells implantation during surgical manipulation.

The time durations from surgery to clinical appearance of metastasis were shown in Table 2. These ranged from one month to 99 months with varying variety of the time interval. The short time duration was shown in patients with pleural involvement and the long time duration was seen in patients with lung metastasis.

According to tnM classification, there were no certain patterns to provoke recurrence as shown in Table 3. The disease stages in patients with recurrence uniformly distributed in terms of tnM classification. It was interest to say that the recurrence more often occurred in patients with stage I or II disease of breast cancer.

The operative procedures used for primary breast cancer were listed in Table 4. Each procedure ensured oncologic radicality as far as possible, including combined operation with
### Table 1. Location and Case

<table>
<thead>
<tr>
<th>Location</th>
<th>Case</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>14</td>
</tr>
<tr>
<td>Pleura</td>
<td>3</td>
</tr>
<tr>
<td>Bone</td>
<td>12</td>
</tr>
<tr>
<td>Liver</td>
<td>5</td>
</tr>
<tr>
<td>Brain</td>
<td>1</td>
</tr>
<tr>
<td>Lymph node</td>
<td>9</td>
</tr>
<tr>
<td>Local skin</td>
<td>14</td>
</tr>
</tbody>
</table>

Including doubles of involved organs

### Table 2. Location, Duration (Average)

<table>
<thead>
<tr>
<th>Location</th>
<th>Duration (Average)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>2~99 (36.1)</td>
</tr>
<tr>
<td>Pleura</td>
<td>2~31 (14.0)</td>
</tr>
<tr>
<td>Bone</td>
<td>10~57 (24.8)</td>
</tr>
<tr>
<td>Liver</td>
<td>1~57 (27.8)</td>
</tr>
<tr>
<td>Lymph node</td>
<td>7~99 (31.9)</td>
</tr>
<tr>
<td>Local skin</td>
<td>1~99 (22.1)</td>
</tr>
</tbody>
</table>

(month)

### Table 3. Factor and Case

<table>
<thead>
<tr>
<th>Factor</th>
<th>Case</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>7</td>
</tr>
<tr>
<td>T2</td>
<td>21</td>
</tr>
<tr>
<td>T3</td>
<td>10</td>
</tr>
<tr>
<td>T4</td>
<td>5</td>
</tr>
<tr>
<td>n0</td>
<td>14</td>
</tr>
<tr>
<td>n1α</td>
<td>7</td>
</tr>
<tr>
<td>n1β</td>
<td>12</td>
</tr>
<tr>
<td>n2</td>
<td>7</td>
</tr>
<tr>
<td>n3</td>
<td>3</td>
</tr>
</tbody>
</table>

### Table 4. CEA Stain

<table>
<thead>
<tr>
<th>CEA Stain</th>
<th>Cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>-</td>
<td>14</td>
<td>(25.9)</td>
</tr>
<tr>
<td>±</td>
<td>4</td>
<td>(7.4)</td>
</tr>
<tr>
<td>+</td>
<td>10</td>
<td>(18.5)</td>
</tr>
<tr>
<td>++</td>
<td>14</td>
<td>(25.9)</td>
</tr>
<tr>
<td>+++</td>
<td>12</td>
<td>(22.2)</td>
</tr>
<tr>
<td>Total</td>
<td>54</td>
<td></td>
</tr>
</tbody>
</table>

### Ploidy

<table>
<thead>
<tr>
<th>Ploidy</th>
<th>Case</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>euploidy</td>
<td>18</td>
<td>(30.0)</td>
</tr>
<tr>
<td>aneuploidy</td>
<td>42</td>
<td>(70.0)</td>
</tr>
<tr>
<td>1.1 ≤ D1 &lt; 1.5</td>
<td>13</td>
<td>(21.7)</td>
</tr>
<tr>
<td>1.5 ≤ D1 &lt; 2.0</td>
<td>21</td>
<td>(35.0)</td>
</tr>
<tr>
<td>2.0 ≤ D1</td>
<td>8</td>
<td>(13.3)</td>
</tr>
</tbody>
</table>

### Table 5. Serum CEA

<table>
<thead>
<tr>
<th>Serum CEA</th>
<th>Cases (Recurrence Rate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>11 (44)</td>
</tr>
<tr>
<td>Normal</td>
<td>14 (56)</td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
</tr>
</tbody>
</table>

Positive: over 4ng/ml

### Table 6. Operative Procedure Cases and Rates

<table>
<thead>
<tr>
<th>Operative Procedure</th>
<th>Cases</th>
<th>Recurrence and Rates**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extended Radical mastectomy</td>
<td>29*</td>
<td>(29/119=24.3)</td>
</tr>
<tr>
<td>Standard mastectomy</td>
<td>8</td>
<td>(8/83=9.6)</td>
</tr>
<tr>
<td>Super-Extended Radical mastectomy</td>
<td>2</td>
<td>(2/7=28.6)</td>
</tr>
<tr>
<td>Limited operation</td>
<td>4</td>
<td>(4/134=3.0)</td>
</tr>
</tbody>
</table>
oophrectomy in three patients. The highest recurrent rate was seen in super- and extended radical mastectomy. Recurrence was more likely to occur in patients who undergo extended-radical mastectomy because these procedures were selected for relatively advanced cancer patients.

The serum CEA levels and a presence of tissue CEA by staining were shown in Table 5. The suggestion is made that high serum CEA level should not indicate an appearance of recurrence following surgical treatment for breast cancer. On the contrary, it is suggested that high tissue CEA enables us to know high possibility to recur.

Table 6 showed a result of an analysis of ploidy patterns in cancer cells according to the method by Schutte. The recurrent rate from cancer cells with aneuploidy was 30 percent although that from aneuploidy was 70 per cent. The highest recurrent rate was shown in aneuploidy in which DI ranged from 1.5 to 2.0.

**DISCUSSION**

In this study, it is clinically evaluated as to whether recurrence of breast cancer could be predicted or not on the basis of the clinical analysis of patients with recurrence.

The predominant recurrent sites are the lung, the local skin and the lymph nodes. However, the disease stages in patients with recurrence were uniformly distributed, not in one-side of the disease stage.

There was a tendency toward occurring recurrence in patients who underwent extended radical mastectomy.

It is a reflection that these procedures are selected for advanced breast cancer patients. The suggestion was made that high tissue CEA content imply high possibility to recur although the serum CEA levels varied.

Black and Fischer reported that cellular atypisms are divided the five stages according to the irregularity, the sizes, the shapes, the staining of nuclei, nucleous and its division. Prognostic factors also have been evaluated in association with histologic findings.

However, objectively histologic finding is mandatory for precise assessment of their prognoses.

Recently advances in flow cytometric techniques enabled physicians to objectively assess the intensity of clinical malignancy in tumor cells. Nishi pointed out that ER positive breast cancers tended to demonstrate the lower DI and RI values. It seems that this fact reflects a hormone-dependent tumors of breast cancer. It is emphasized that assessment of biologic patterns in breast cancers helps determine the validity of chemoendocrine therapy in follow-up courses.

On the other hand, the serum CEA levels are now utilized widely as a clinical marker.

In case of breast cancer, serum CEA is too low to be useful for screening. It, however, is accepted that high serum CEA levels help us forecast recurrence and special attention focused on serum CEA as a prognostic factors and the evaluation of therapeutic efficacy.

In this series, the serum CEA level failed to closely correlate with forecasting recurrence. On the other hand, tissue CEA level by staining in cancer tissues correlated with recurrence as an index of in cancer tissues correlated with recurrence as an index of prognosis. It is well known that the prognosis of CEA-negative tumors is better than CEA-positive one.

In breast cancer, the clinical value of tissue-CEA is still controversial, with some reports of a poorer prognosis in CEA positive patients and others of not showing prognostic correlation. In this study, there was a certain prognostic correlation between tissue CEA and recurrence. It seems reasonable to emphasize that CEA production is an intrinsic biological characteristic of the tumor.

Kuhajda reported that CEA-positive tumors are more likely to show metastasis, particularly severe metastasis. It is certain that tissue CEA-positive tumors show a biologically malignant behavior to present local and distant metastases and recur in early stage following surgery. Tissue CEA was positive in 96.3% of patients with recurrence, in contrast, high serum CEA was positive in 44% of them in this series.

The expression of tissue CEA is associated with a high incidence of recurrence in anticipation of a poor outcome.
REFERENCES


