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Risk Factor for Recurrence of Breast Cancer

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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 metastastasis to the lung and the liver in 70% of patients and 50% of bone metastasis. As the symptomes 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 reucrrent 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 favarable 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 reucrrence 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 for as possible, including combined operation with

Tacle 1.

location	case
lung	14
pleura	3
bone	12
liver	5
brain	1
lymph node	9
local skin	14

including doubles of involved organs

Tacle 2.

location	duration (average)
lung	2~99 (36.1)
pleura	2~31 (14.0)
bone	10~57 (24.8)
liver	1~57 (27.8)
lymph node	7~99 (31.9)
local skin	1~99 (22.1)

(month)

Tacle 3.

factor		case
T1		7
T2		21
T3		10
T4		5
n0		14
n1α		7
n1β		12
n2		7
n3		3
stage	I	14
	II	12
	III	11
	IV	5

Tacle 4. CEA stain

CEA stain	cases	%
−	14	(25.9)
±	4	(7.4)
+	10	(18.5)
++	14	(25.9)
+++	12	(22.2)
Total	54	

Ploidy

Ploidy	case	(%)
euploidy	18	(30.0)
aneuploidy	42	(70.0)
1.1 ≦ DI < 1.5	13	(21.7)
1.5 ≦ DI < 2.0	21	(35.0)
2.0 ≦ DI	8	(13.3)

Table 5. Serum CEA

Serum CEA	cases (recurrene rate)
Positive	11 (44)
normal	14 (56)
Total	25

positive: over 4ng/ml

CEA Stain

Staning rate		case	(%)
0%	−	1	(3.7)
~20%	+	17	(63.0)
~50%	++	6	(22.2)
80%~	+++	3	(11.1)
Total		27	

Table 6.

operaive procedure	cases	recurrence and rates**
extended radical mastectomy	29*	(29/119=24.3)
standard mastectomy	8	(8/ 83= 9.6)
super-extende radical mastectomy	2	(2/ 7=28.6)
limited operation	4	(4/134= 3.0)

*

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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 tissuse 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 suggeted that high tissuse CEA enables us to know high possibility to recur.

Table 6 showed a result of an analysis of ploidy patterns in cancer cells accroding to the method by Schutte[1]. 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 reucrrence 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 reflestion that these procedures are selected for advanced breat cancer patients. The suggestion was made that high tissue CEA content imply high possibility to recur although the serum CEA levels varied.

Black[2, 3] and Fischer[4] 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[5].

Nishi[6] 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[7, 8] and the evaluation of therapeutic efficacy[9].

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 tissuses 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[10].

In breast cancer, the clinical value of tissue-CEA is still controversial, with some reports of a poorer prongnosis in CEA positive patients[11] and others of not showing prognostic correlation[12]. In this study, there was a certain prognostic correlation between tissue CEA and recurrence. It seems reasonable to emphasize that CEA producition is an intrinsic biological characteristic of the tumor.

Kuhajda[13] reproted 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 contarst, 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

1) Schutte B, Reynders MMJ, Bosman FT *et al*: Flow cytometric determination of DNA ploidy level in nuclei isolated from paraffin-embedded tissue. *Cytometry* **6**: 26-30, 1985.
2) Black MM, Opler SR, and Speer FD: Survival in breast cancer cases in releation to the structure of the primary tumor and regional lymph nodes. *Surg Gynecol Obstet* **100**: 543-551, 1955.
3) Black MM, Speer FD, and Opler SR: Structural representations of tumor-host relationship in mammary carcinoma. Biologic and Prognostic Significance. *Am J Clin Pathol* **26**: 250-265, 1956.
4) Fischer ER, Redmond C, and Fishcer B: Histologic grading of breast cancer. pathol *Annu Part* **1**: 239-251, 1980.
5) Volm M, Hahn EW and Mattern J: Five year follow-up study of independent clinical and flow cytometric prognostic factors for the survival of patiens with non-small cell lung carcinoma. *Cancer Res* **48**: 2923-2928, 1988.
6) Nishi R: Cellular DNA content in breast cancer —in relation to hormone receptor and nuclear atypism— *Oaska Med J* **44**: 422-435, 1985.
7) Wan DY, Knyba RE, Bulbrook RD *et al*: Serum carcinoembryonic antigen in the diagnosis and prognosis of women with breast cancer. *Eur J Cancer Clin Oncol* **20**: 25-31, 1984.
8) Mughal AW, Hortobagyi GN, Fritsche HA *et al*: Serial plasma carcinoembryonic antigen measurements during treatment of metastatic breast cancer. *JAMA* **249**: 1881-1886, 1983.
9) Haga S, Kajiware T, Haga Y, Shimizu T *et al*: Clinical study on serum and tissue CEA for the recurrence of breast cancer. *Jpn J Asso Clin Surg* **48**: 1029-1034, 1987.
10) Ikeda E, Kojima O, Tanioku T, Kitagawa N *et al*: Relationship of prognosis of gastric cancer patients to the staining for carcinoembryonic antigen (CEA) in gastric cancer. *Jpn J Gastroenterol Surg* **16**: 1638-1644, 1983.
11) Mansour EG, Haster M, Park CH *et al*: Tissue and plasma carcinoembryonic antigen in early breast cancer. *A prognostic factor cancer* **51**: 1243-1248, 1983.
12) Smith SR, Howell A, Minawa A *et al*: The clinical value of immunohistologically demonstrable CEA in breast cancer: A possible method of selecting patients for adjuvant chemotherapy. *Br J Cancer* **46**: 757-764, 1982.
13) Kuhajda FP, Offut LE, Mendelsohn G: The distribution of carcinoembryonic antigen in breast carcinoma. Diagnostic and prognostic implications. Cancer **52**: 1259-1246, 1983.