Serum C-erbB-2 Protein in Breast Cancer Patients

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Abstract

Measurements of c-erbB-2 protein were done in sera of 20 normal women, 22 benign breast disease patients and in respectively 43 and 51 samples from primary breast cancer patients obtained prior to and after surgical interventions. Mean value of serum c-erbB-2 in non-malignant women was insignificantly different from the value in the breast cancer group. Positivity rate of serum c-erbB-2 in the cancer group was 13.8 per cent. Increasing postoperative serum c-erbB-2 concentrations were in good association with severity, progressiveness and relapse of breast cancer independently of other variables such as age, menopausal status, tumor size, axillary node invasion, ER or PR status. Pretreatment serum c-erbB-2 positivity was inversely correlated to ER status but relation to other prognostic parameters of breast cancer was not found. Agreement between c-erbB-2 measured in serum by enzymeimmunoassay and in tissue by immunohistochemical assay was also found.

Our data confirmed that in primary breast cancer patients, monitoring of circulating c-erbB-2 protein levels after operation are useful for detecting the recurrence and/or metastasis of the disease especially in ER positive breast cancer. Pretreatment serum c-erbB-2 concentrations do not have benefit for early diagnosis of the tumor.

Key word : Serum c-erbB-2 Protein, Primary Breast Cancer

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Alterations of proto-oncogenes contribute to the pathogenesis of cancer. A proto-oncogene in human breast cancer, c-erbB-2, has been intensively studied. It is located on chromosome 17 q 21 and encodes a 185-kD transmembrane glycoprotein similar to that of the epidermal growth factor receptor[1]. The extracellular domain of c-erbB-2 can be shed by proteolytic clevage from cancer cells in cultures that overexpress p 185 c-erbB-2[2,3]. C-erbB-2 protein can be detected in human serum with breast cancer[3-6] and several investigations indicate that c-erbB-2 may be a useful prognostic serum marker in primary breast cancer[7-12]. This study aimed to evaluate the prognostic significance of serum c-erbB-2 in Thai women with primary breast cancer.

PATIENTS AND METHOD

Patients

Sera form 94 patients with primary breast cancer were investigated. Forty three blood samples were drawn before giving any kind of treatment and 51 samples were obtained after surgical treatment. Most of the patients in the latter group had already received different therapeutic regimens (e.g. hormone therapy, chemotherapy and/or radiotherapy). Blood from 20 healthy women and 22 patients with benign breast disease was also obtained. Centrifugation of blood was done immediately after drawing and the sera were stored at -70°C until the measurement of c-erbB-2 was performed.

Estrogen and progesterone receptor status was determined in tumor tissue using enzymimmunoassay (Abbott Laboratory) and control-pore glass bead ligand binding assay respectively. Cutoff level of ER was 15 fmol/mg protein and for PR was 10 fmol/mg protein. Median follow-up time of breast cancer patients was 49.5 months (range : 7-123 months). For the diagnosis of metastasis, clinical examinations were performed every 3-6 months and chest X-ray, liver scans or ultrasonography and bone scans were done every 6-12 months.

C-erbB-2 measurement

Determination of serum c-erbB-2 was done using enzymimmunoassay kits kindly donated by Nichirei Corporation, Japan. The assay was based on the two step sandwich technique using two mouse monoclonal anti c-erbB-2 antibodies. First antibody which was immobilized on the polystyrene bead reacted with c-erbB-2 in the serum sample. After 2 h incubation at room temperature, unreacted c-erbB-2 was removed by washing, then, another enzyme-conjugated mouse monoclonal antibody was added to bind with c-erbB-2 first-antibody complex coated on the bead. Unreacted enzyme-conjugated second antibody was removed by washing after 2 h incubation at room temperature and enzyme reaction was started by adding chromogenic substate. The absorbance of developed color which was correlated with c-erbB-2 concentration in sample was measured after 30 min reaction at room temperature and calculation of c-erbB-2 concentration was performed by comparison with standards. As proposed in the protocol, the inter-and intra-assay reproducibility was 8.7 to 9.7 per cent and 2.15 to 6.7 per cent respectively. The sensitivity of the assay was 0.5 ng/ml and a tentative cutoff value at 5.4 ng/ml was recommended in the kit. Thirty three breast cancer tissues from 94 patients were also measured for tissue c-erbB-2 expression by immunohistochemical technique.

Statistics

C-erbB-2 concentrations and other descriptive data were presented in mean ± SEM. The relationship between c-erbB-2 serum concentrations and other clinico-pathological variables were evaluated by non-parametric comparison. The serum positivity rate was compared to various nominal variables by Chi square test and the odds ratios for relapse i.e. recurrence and/or metastasis were calculated. Logistic regression was used to analyzed the predictive value of serum c-erbB-2 when other prognostic variables of breast cancer were adjusted. Statistical analysis was performed by statview-PC program except the logistic regression which was done by SPSS-PC program and significance was set at p value less than 0.05.

RESULTS

Mean age of the women in the apparently healthy group and benign breast disease (BBD) group was 31.25 ± 0.86 and 35.09 ± 2.42 years respectively. Patients with primary breast cancer had a mean age 50.13 ± 1.12 years. Mean concentration and per cent positivity at 5.4 ng/ml cutoff value of serum c-erbB-2 in each studied group is tabulated in Table 1. Mean serum c-erbB-2 level in non-malignant group (normal + BBD) was 2.15 ± 0.58 ng/ml which did not significantly differ from value

Table 1. Serum c-erbB-2 levels and positivity rate in each group of subjects.

N		Mean (SE)		(Min-Max)	P value	% Positive	P value
Non-malignant group	42	2.15	(0.58)	(0 - 5.25)		4.8 (2/42)	
Normal	20	2.22	(0.87)	(0 - 4.50)	0.86(a)	5.0 (1/20)	0.94(a)
Benign breast disease	22	2.09	(0.79)	(0 - 5.25)		4.5 (1/22)	
Malignant breast tumor	94	8.59	(3.19)	(0 - 199.35)	0.77(b)	13.8 (13/94)	0.12(b)

(a) Normal vs benign breast disease
(b) Malignant vs non-malignant groups

8.59 ± 3.19 ng/ml in malignant breast tumors. Distribution of c-erbB-2 in sera of non-malignant and malignant subjects is shown in Fig. 1. Positivity rate of c-erbB-2 among the three groups was also not different.

Various clinico-pathological variables were used for comparison of c-erbB-2 concentrations and positivity as shown in Table 2. Mean level of c-erbB-2 in the pretreatment group of breast cancer patients was higher than the value in postoperative patients but positivity was not different between the two groups. Progressive increase of postoperative c-erbB-2 concentrations and positivity rate followed the advance of disease as seen in different stages of breast cancer with the highest value in stage 4 or metastatic breast cancer was detected. (Fig. 2) In addition, statistically higher

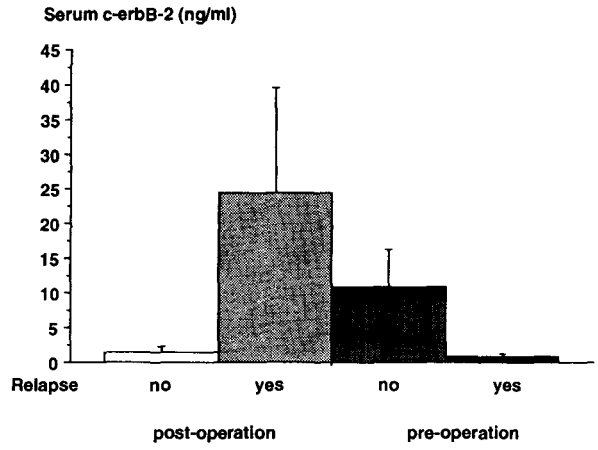

Fig. 2. Postoperative serum c-erbB-2 concentrations in different stages of breast cancer.

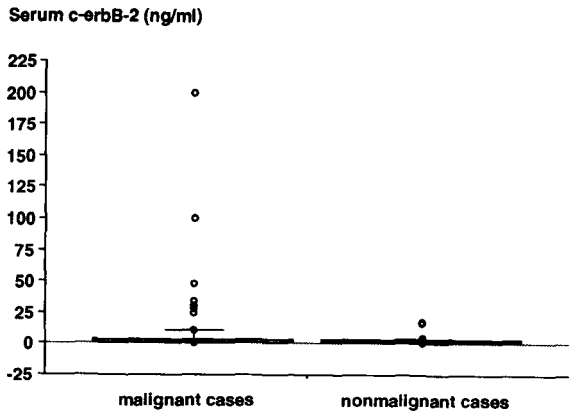

Fig. 1. Serum c-erbB-2 concentrations in malignant breast tumor and non-malignant (normal + benign breast disease) group.

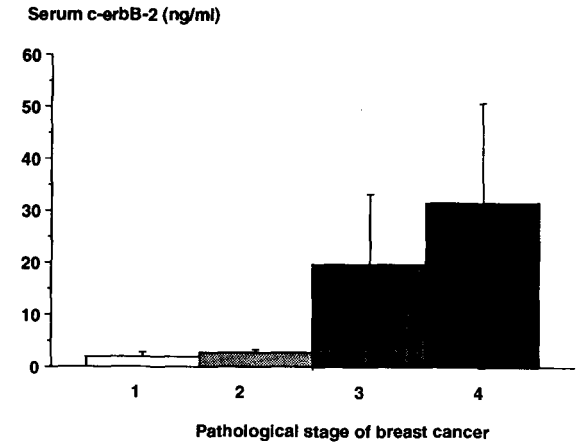

Fig. 3. Bar chart of c-erbB-2 levels in preoperative and postoperative serum samples obtained from breast cancer patients with and without relapse.

Table 2. Concentrations and positivity of serum c-erbB-2 in relation to clinico-pathological characteristics of breast cancer patients.

	Mean (SE)	P value	% Positive	Chi square P value
Obtained-blood samples				
Pre-treatment	10.04 (5.11)	0.01	11.6	0.57
Post-operation	7.37 (4.04)		15.7	
*Tumor stage				
1	3.28 (2.89)	0.01	33.3	0.0002
2	1.35 (0.91)		3.2	
3	0.84 (0.38)		0	
4	31.59 (19.31)		60.0	
*Cancer progresiveness				
< 3 lymph node invasion	1.04 (0.41)	0.01	4.5	0.0003
> 3 lymph node invasion	2.28 (1.75)		6.3	
Distant metastasis	31.59 (19.31)		60.0	
*Relapse				
No	1.56 (0.77)	0.02	5.3	0.0005
Yes	24.36 (15.15)		46.2	

*Post-operative values only

Table 3. Relationship between c-erbB-2 positivity rate in serum or tissue with estrogen receptor status in breast cancer patients.

		Serum c-erbB-2(%)				Tissue c-erbB-2 expression (%)	
		Pre-treatment		Post-operation			
		Positive	Negative	Positive	Negative	Positive	Negative
ER	Positive	0	100	18.2	81.8	25.0	75.0
	Negative	23.5	76.5	9.1	90.9	69.2	30.8
N		40		22		33	
Chi square p value		0.01		0.53		0.01	

mean concentration and per cent positivity of post-operative serum c-erbB-2 in relapse patients compared to non-relapse cases was detected. (Table 2 and Fig. 3) Significant relationship of elevated c-erbB-2 protein concentrations with age, menopausal status, tumor diameter, axillary node invasion, ER and PR status was observed neither in pretreatment nor in postoperative serum samples of breast cancer patients.

Reverse relationship between ER and tissue c-erbB-2 status as well as between ER status and pretreatment serum c-erbB-2 concentrations was demonstrated (Table 3) but postoperative serum c-erbB-2 levels were not related to ER status. Table 4 shows the incidence of relapse breast cancer in relation to ER and serum c-erbB-2 status. Highest incidence of relapse was seen in patients having positive findings for both ER and c-erbB-2 though significance was not achieved.

Good agreement of c-erbB-2 expression in 33 breast cancer tissues with pre-operative status of serum c-erbB-2 protein was found in patients having elevated serum c-erbB-2 values (Table 5). However, the discordance between tissue and serum c-erbB-2 in patients with negative serum c-erbB-2 was approximately 36 per cent. The odds ratios of recurrence and/or metastasis of breast cancer were calculated. (Table 6) With the limited cases of relapse (16/94) in our data, elevated serum c-erbB-2 was the only factor that significantly increased the risk of recurrence and/or metastasis in primary breast cancer. For other variables, the odds ratio of 1 was included in their ranges which made their relationship with relapse of the disease to be insig-

Table 4. Incidence of relapse breast cancer in relation to ER and serum c-erbB-2 status.

ER	C-erbB-2	% Relapse cases	
Negative	Negative	8.7	(2/23)
Negative	Positive	0	(0/5)
Positive	Negative	9.4	(3/32)
Positive	Positive	50	(1/2)

Chi square p value > 0.05, N = 62

Table 5. Relationship between pretreatment serum c-erbB-2 and tissue c-erbB-2 in breast cancer patients.

		Serum c-erbB-2 (%)	
		Positive	Negative
Tissue c-erbB-2(%)	Positive	100	36.7
	Negative	0	63.3

Chi square p value = 0.03, N = 33

Table 6. Odds ratios for predicting occurrence of relapse in primary breast cancer.

Variable		Relapse/total cases (%)	Odds ratio (95% CI)	P value
Age	≤ 50 y	8/44 (18.2)	1(a)	0.81
	> 50 y	8/49 (16.3)	0.9 (0.3-2.6)	
Tumor diameter				
	≤ 20 mm	1/17 (5.9)	1(a)	0.34
	> 20 mm	10/67 (14.9)	2.8 (0.3-23.6)	
Lymph node invasion				
	no	4/35 (11.4)	1(a)	0.83
	yes	6/46 (13.0)	1.2 (0.3-4.5)	
(b) Tissue c-erbB-2				
	negative	3/19 (15.8)	1(a)	0.90
	positive	0/14 (0)	0	
Serum c-erbB-2				
	negative	10/81 (12.3)	1(a)	0.005
	positive	6/13 (46.2)	6.1 (1.7-21.8)	
(b) ER	negative	2/28 (7.1)	1(a)	0.54
	positive	4/34 (11.8)	1.7 (0.3-10.2)	
(b) PR	negative	5/49 (10.2)	1(a)	0.91
	positive	1/11 (9.1)	0.9 (0.1-8.4)	

(a) Taken as reference category

(b) Results may not be applicable due to the small number of relapse cases.

nificant. However, when other variables were adjusted, the significance of serum c-erbB-2 for independently predicting relapse of breast cancer disappeared.

DISCUSSION

Serum c-erbB-2 levels and positivity rate were not different among normal women, BBD and breast cancer patient groups. The levels of c-erbB-2 in serum drawn before surgery was significantly higher than in serum obtained after surgery. Thus, data analysis was separately done according to time of blood taken. By using the value above 5.4 ng/ml for indicating the positivity of c-erbB-2 in serum, Thai women with primary breast cancer had 13.8 per cent positivity rate of serum c-erbB-2. This agrees with the positivity value 8.6-15 per cent previously reported in other nationalities[4,7,8,10,12]. Age and menopausal status had no influence on c-erbB-2 protein concentrations in our patients as reported before[11,13,14]. Neither tumor size nor axillary lymph node invasion was associated with serum c-erbB-2 positivity which was similar to findings in several studies[10,11,14-16] but not others[12].

It was suggested that the primary tumor is a major source of c-erbB-2 protein, so that significance of circulating c-erbB-2 levels in assessing the extent of the spread of cancer should be performed in blood samples obtained after the removal

of primary breast cancer[13]. Postoperative levels and positivity rate of serum c-erbB-2 in the present study were significantly different among breast cancer stages as well as between relapse and non-relapse patients. Stage 4 breast cancer patients in this study had the highest mean level and per cent positivity (60%) of serum c-erbB-2 compared to the other three earlier stages. Previous literature reported a range of 21-49 per cent positivity in stage 4 patients[4,12,14,15-20]. Pretreatment serum c-erbB-2 showed no relationship with tumor stages or any parameters indicating the advance of the disease. Most authors, including us agreed that serum c-erbB-2 protein was useful as an indicator of post-operative follow-up for tumor aggressiveness but not as a diagnostic marker of primary breast cancer [3,5,14,17,21]. However, significance of serum c-erbB-2 for selecting the early stage patients with a worse prognosis in terms of shorter disease free interval and survival outcome was also reported [10,18,20]. In addition, elevated pretreatment c-erbB-2 in serum of ER positive metastatic breast cancer patients was shown to be associated with low probability of benefit from various types of hormone therapy[11,13,22]. Thus, it was recommended to add positive preoperative serum c-erbB-2 as one parameter in the decision for high-dose chemotherapy in locoregional advanced breast cancer patients[11,22].

In this study, ER and PR status did not significantly relate to postoperative serum c-erbB-2 status. Contradictory, reverse association between ER and pretreatment serum c-erbB-2 as well as tissue c-erbB-2 expression was obtained. Our results are in agreement with some authors[10,11] but not with others who found no relationship between steroid receptors and serum c-erbB-2 protein[12,15]. Among very limited cases of relapse in our study, 50 per cent of patients with relapse had positive ER and c-erbB-2 protein while about 9 per cent of relapse cases occurred in patients having positive ER but negative c-erbB-2 protein. Though the significance was not achieved, this may support a previous suggestion that in ER positive breast cancer, elevated serum c-erbB-2 protein was associated with a higher risk of relapse[11].

Positive association between serum and tissue c-erbB-2 was shown in our study as in most previous reports[7,10,12,16,17] but not by some authors[15]. However, some discordance between serum and tissue c-erbB-2 expression was also shown by other groups of investigators[15,18] including us. About 36 per cent of our patients with negative pretreatment serum c-erbB-2 protein had positive tissue c-erbB-2 expression. This may be related to the difference in sensitivity of the measuring methods or that the serum component represents an alternatively spliced variant lacking the membrane domain[15]. Insignificant relationship between positive tissue c-erbB-2 expression and relapse rate was observed.

Positive serum c-erbB-2 seems to be the only significant prognostic indicator for relapse of breast cancer from our limited data with an odds ratio of 6.1 (range 1.7-21.8) in comparison to patients with negative serum c-erbB-2 levels, although, the significance disappeared when other prognostic variables were adjusted. This should be confirmed using a larger group of patients and longer follow-up time. Also, our results may support an earlier suggestion that monitoring of post-operative serum c-erbB-2 protein offers important value for detecting advanced breast cancer no matter if the tissue c-erbB-2 is present or absent [5,15,16]. Previous reports from two groups of investigators revealed that elevated serum c-erbB-2 concentrations could predict the appearance of recurrence or metastasis within 3-9 months[8,16].

In conclusion, c-erbB-2 measurement in serum of breast cancer patients after surgical treatment provides a good indicator of progressiveness and relapse of the disease independently of other prognostic factors such as tumor size or axillary node invasion. An ER positive tumors with elevated serum c-erbB-2 levels showed a higher incidence of relapse than tumors with low circulating c-erbB-2 levels. Monitoring of postoperative serum c-erbB-2 should be a useful tool for early detection of relapse in ER positive breast cancer.

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REFERENCES

1. Maguire HC, Green MI. The neu (c-erbB-2) oncogene. Semin Oncol 1989; 16:148-55.
2. Zabrecky JR, Lam T, McKenzie SJ, Carney W. The extracellular domain of p185 neu is released from the surface of human breast carcinoma cell, SK-BR-3. J Biol Chem 1991; 266:1716-20.
3. Pupa SM, Menard S, Morelli D, Pozzi B, De Palo G, Calnaghi MI. The extracellular domain of the c-erbB-2 oncoprotein is released from tumor cells by proteolytic clevage. Oncogene 1993;8:2917-23.
4. Carney WP, Hamer PJ, Petit D, et al. Detection and quantitation of the human neu oncoprotein. J Tumor Marker Oncol 1991; 6:53-72.
5. Kynast B, Binder L, Marx D, et al. Determination of c-erbB-2 translational product p185 in serum of breast cancer patients. J Cancer Res Clin Oncol 1993; 199:249-52.
6. Leitzel K, Teramoto Y, Sampson E, et al. Elevated soluble c-erbB-2 antigen levels in the serum and effusions of a proportion of breast cancer patients. J Clin Oncol 1992; 10:1436-43.
7. Narita T, Funahashi H, Satoh Y, Takagi H. C-erbB-2 protein in the sera of breast cancer patients. Breast Cancer Res Treat 1992; 24:97-102.
8. Isola JJ, Holli K, Oksa H, Teramoto Y, Kallioniemi OP. Elevated c-erbB-2 oncoprotein levels in preoperative and follow-up serum samples define an aggressive disease course in patients with breast cancer. Cancer 1994; 73:652-8.
9. Leitzel K, Teramoto Y, Konrad K, et al. Elevated c-erbB-2 antigen levels and decreased response to hormone therapy of breast cancer. J Clin Oncol 1995; 13:1129-35.
10. Molina R, Jo J, Filella X, et al. C-erbB-2 oncoprotein in the sera and tissue of patients with breast cancer: utility in prognosis. Anticancer Res 1996; 16:295-300.
11. Fehm T, Maimonis P, Weitz S, Teramoto Y, Katalinic A, Jager W. Influence of circulating c-erbB-2 serum protein on response to adjuvant chemotherapy in node-positive breast cancer patients. Breast Cancer Res Treat 1997; 43:87-95.
12. Krainer M, Brodowicz T, Zeillinger R, et al. Tissue expression and serum levels of Her-2/neu in patients with breast cancer. Oncology 1997; 54:475-81.
13. Mehta RR, McDermott JH, Heiken TJ, et al. Plasma c-erbB-2 levels in breast cancer patients: prognostic significance in predicting response to chemotherapy. J Clin Oncol 1998;16:2409-16.
14. Kath R, Hoffken K, Otte C, et al. The neu-oncogene product in serum and tissue of patients with breast carcinoma. Ann Oncol 1993;4:585-90.
15. Kandl H, Seymour L, Bezwoda WR. Soluble c-erbB-2 fragment in serum correlates with disease stage and predicts for shortened survival in patients with early-stage and advanced breast cancer. J Cancer 1994;70:739-42.
16. Mansour OA, Zekri AR, Harvey J, Taramoto Y, El-Ahmady O. Tissue and serum c-erb B-2 and tissue EGFR in breast carcinoma: three years follow-up. Anticancer Res 1997; 17:3101-6.
17. Fehm T, Maimonis P, Katalinic A, Jager WH. The prognostic significance of c-erbB-2 serum protein in metastatic breast cancer. Oncology 1998; 55: 33-8.
18. Willsher PC, Beaver J, Pinder S, et al. Prognostic significance of serum c-erbB-2 protein in breast cancer patients. Breast cancer Res Treat 1996; 40:251-5.
19. Molina R, Jo J, Zanon G, et al. Uitlity of c-erbB-2 in tissue and in serum in the early diagnosis of recurrence in breast cancer patients : comparison with carcinoembryonic antigen and CA 15-3. Br J Cancer 1996; 74:1126-31.
20. Yamauchi H, Neill AN, Gelman R, et al. Prediction of response to antiestrogen therapy in advanced breast cancer patients by pretreatment circulating levels of extracellular domain of the HER-2/c-neu protein. J Clin Oncol 1997; 15:2518-25.
21. Volas GH, Leitzel K, Teramoto Y, Grossberg H, Demer SL, Lipton A. Serial serum c-erbB-2 levels in patients with breast cancer. Cancer 1996; 78: 267-72.
22. Muss HB, Thor AD, Berry DA, et al. C-erbB-2 expression and response to adjuvant therapy in women with node positive early breast cancer. N Engl J Med 1994;330:1260-6.

ซีรัม ซีเอิร์บบีสองโปรตีนในผู้ป่วยมะเร็งเต้านม

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น้ำอ้อย กลิ่นสละ, วท.บ., ศศิธร สังขบุญชู, ป.พวก.**

ได้ทำการวัดซีเอิร์บบีสองโปรตีน ในซีรั่มหญิงไทยปกติ 20 ราย, ผู้ป่วยโรคเต้านมชนิดไม่ร้ายแรง 22 ราย และผู้ป่วยมะเร็งเต้านมชนิดปฐมภูมิ ซึ่งเจาะเลือดก่อนการรักษา 43 ราย และหลังผ่าตัด 51 ราย ค่าเฉลี่ยของซีเอิร์บบีสองในสตรีซึ่งไม่เป็นมะเร็งเต้านมไม่แตกต่างจากกลุ่มมะเร็งเต้านมอย่างมีนัยสำคัญ พบค่าสูงผิดปกติในผู้ป่วยมะเร็งเต้านม 13.8 เปอร์เซ็นต์ ค่าบวกของซีเอิร์บบีสองในเลือดที่เจาะหลังผ่าตัดสัมพันธ์ดีกับปัจจัยบ่งความรุนแรงและการลุกลามของโรค รวมทั้งการกลับเป็นซ้ำของโรคมะเร็งเต้านม โดยไม่ขึ้นกับปัจจัยเสี่ยง เช่น อายุ, ภาวะหมดประจำเดือน, ขนาดก้อนมะเร็ง, การลุกลามไปยังต่อมน้ำเหลือง, ปริมาณตัวรับเอสโตรเจนหรือตัวรับโปรเจสเตอโรน ค่าบวกของซีเอิร์บบีสองในซีรัมที่เจาะก่อนให้การรักษาแปรผกผันกับค่าบวกของตัวรับเอสโตรเจน โดยไม่สัมพันธ์กับปัจจัยพยากรณ์โรคอื่น ๆ ค่าซีเอิร์บบีสองซึ่งวัดในเลือดโดยวิธีเอ็นซัยม์อิมมูโนเอสเสย์ และในเนื้อมะเร็งเต้านมโดยวิธีอิมมูโนฮีสโตเคมี มีความสอดคล้องกันดี

ผลการวิจัยสนับสนุนว่าการวัดซีเอิร์บบีสองในเลือดผู้ป่วยมะเร็งเต้านมสตรีภายหลังการผ่าตัดรักษา มีประโยชน์สำหรับบอกการกลับเป็นซ้ำหรือการกระจายของโรค โดยเฉพาะอย่างยิ่งในมะเร็งเต้านมที่ตรวจพบตัวรับเอสโตรเจน การวัดซีเอิร์บบีสองในเลือดก่อนให้การรักษา ไม่มีประโยชน์สำหรับให้การวินิจฉัยโรคมะเร็งเต้านมสตรีระยะเริ่มแรก

คำสำคัญ : ซีรัม ซีเอิร์บบีสอง, มะเร็งเต้านมปฐมภูมิ

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