Role of serum carcinoembryonic antigen (CEA) as a tumor marker in breast cancer

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ABSTRACT

Background: There is a need for biological prognostic indicators in breast cancer that would, alone or in combination with others, be sufficient to predict disease recurrence and, hence, be the basis for supplemental treatment after local therapy. Aims: To investigate the association between tumor marker serum carcinoembryonic antigen (CEA) and clinicopathological parameters in patients with breast cancer. Methods: A total of 134 patients with breast cancer treated in a single general surgery unit between January 2012 and November 2013 were included in the study, with age ranging between 28 and 73 years. Serum CEA values were compared before and after the treatment of breast cancer, between different histological types of breast cancer patients, between axillary lymphnode-positive and axillary lymphnode-negative patients, and between premenopausal and postmenopausal breast cancer patients. Data were analyzed using the statistical software SPSS version 19. Results: There was significant change in the values of serum CEA before (10.71 ± 2.79 ng/ml) and after the surgery for breast cancer (9.73 ± 3.00 ng/ml) (P < 0.006). There was further decline in the serum CEA level after a course of chemo-radiotherapy (7.30 ± 2.79 ng/ml) (P < 0.001). There was no significant difference between the different histological types of breast cancer (P value 0.55). The difference was significant in patients who were axillary lymphnode positive and negative (P value 0.001). There was no significant difference in premenopausal and postmenopausal breast cancer patients (P value 0.86). Conclusions: Serum CEA is a tumor marker of breast carcinoma. Its level decreased after treatment. This decrease is found more after chemo/radiotherapy following surgery. Serum CEA values are found to be elevated in patients with axillary lymphnode metastasis. There is no significant relation with the histologic type of breast cancer and menopausal status of the patient.

Key words: Axillary lymphnodes, breast cancer, carcinoembryonic antigen, histological type, menopausal status

INTRODUCTION

Breast cancer is the most common cause of death in middle-aged women in western countries. Despite all advances and modifications in treatment modalities, the incidence of breast cancer remains to be unchecked with increasing rate and unchanged mortality rate and is also creating grave morbidity and immense psychological problems for the survivors. This necessitates better understanding of biology of breast cancer, its origin and progression, which will permit the effective management of its treatment, detection, and perhaps even its prevention.

There is a need for biological prognostic indicators that would, alone or in combination with others, be sufficient to predict disease recurrence and, hence, be the basis for supplemental treatment after local therapy. In this effort toward better understanding, currently major studies have been conducted on the immunological aspects of
breast cancer to delineate a specific biological marker. Among the various biological markers detected so far, carcinoembryonic antigen (CEA) has been found to be one of the very important and most commonly expressed biological markers in breast cancer patients.\[1\]

CEA is a high molecular weight (200 kDa) cell surface glycoprotein.\[2\] It was first discovered by Gold and Freedmann.\[3\] Normal levels are observed in benign diseases and elevated levels are found in colon cancer, breast cancer, lung cancer, hepatocellular carcinoma, etc.\[4\] Elevated plasma levels of serum CEA are related to the extent of the disease, degree of differentiation of the tumor, and site of metastasis.\[5\] We undertook this study to determine the changes in the level of serum CEA in breast cancer patients before and after the treatment (surgery/chemo-radiotherapy) between different histological types of breast cancer patients, between axillary lymphnode-positive and axillary lymphnode-negative patients, and between premenopausal and postmenopausal breast cancer patients.

**METHODS**

**Type of study: Prospective**

**Inclusion criteria**

1. All the patients presenting to the OPD and diagnosed as having breast cancer either by core needle biopsy or fine needle aspiration cytology (FNAC) were included in the study.
2. Patients who were having positive axillary lymphnodes during the surgery were included in the study.

**Exclusion criterion**

Patients who were having distant metastasis or involvement beyond the axillary lymph nodes were excluded from the study.

**Patients’ information**

A total of 134 patients with breast cancer treated in a single general surgery unit between January 2012 and November 2013 were included in the study. The age of the patients ranged from 28 to 73 years. The diagnosis of breast cancer was made by core needle biopsy. The patients were divided into two groups on the basis of histological type of breast cancer (126 patients had infiltrating ductal carcinoma and 8 patients had infiltrating lobular carcinoma), axillary lymphnode status (positive in 97 patients and negative in 37 patients), and menopausal status of the patient (53 premenopausal patients and 81 postmenopausal patients).

**Serum collection and tumor markers measurement**

Blood samples from these patients were collected in plain sterile vial without additives or anticoagulants and sera obtained after centrifugation were subjected to CEA analysis by microplate chemiluminescence method at the following stages:

1. Preoperative
2. Postoperative
3. After a course of chemo- and radiotherapy, CEA levels were compared using paired t-test.

**Statistical analysis**

Comparisons were done between the groups using paired t-test. Antigen levels are expressed as mean ± SD. Two-tailed P-values <0.05 were considered as statistically significant. Probabilities were calculated with one degree of freedom. All calculations were made using SPSS version 19.

**RESULTS**

Serum CEA levels were assessed before surgery, after surgery, and after a course of chemo-radiotherapy [Tables 1 and 2]. Preoperative baseline value of serum CEA was 10.71 ± 2.79 ng/ml, which decreased to 9.73 ± 3.00 ng/ml after the surgery (P value 0.006). There was further significant decrease in the level of serum CEA after a course of chemo-radiotherapy (7.30 ± 2.79 ng/ml) (P < 0.001).

Table 3 shows the comparison of the level of serum CEA between the different histological types of breast cancer. Out of 134 patients who were included in the study, there were 126 patients with infiltrating ductal carcinoma and 8 patients with infiltrating lobular carcinoma. Mean ± SD value of serum CEA in patients with infiltrating ductal carcinoma was 10.23 ± 2.58 ng/ml and in patients with lobular carcinoma was 9.65 ± 3.84 ng/ml (P value 0.55).

| Table 1: Comparison of pretreatment and post-treatment values of CEA in breast cancer patients |
|---------------------------------------------------------------|
| Mean preoperative value of serum CEA ± SD (ng/ml) (n = 134) | Mean postoperative value of serum CEA ± SD (ng/ml) (n = 134) | P value |
| 10.71±2.79 | 9.73±3.00 | 0.006 |

| Table 2: Comparison of postoperative values of serum CEA with the values after chemo-radiotherapy |
|----------------------------------------------------------------------------------------|
| Mean postoperative value of serum CEA ± SD (ng/ml) (n = 134) | Mean value of serum CEA after chemo-radiotherapy ± SD (ng/ml) (n = 134) | P value |
| 9.73±3.00 | 7.30±2.79 | <0.001 |

| Table 3: Comparison of CEA levels in different histological types of breast cancer patients |
|----------------------------------------------------------------------------------------|
| Mean value of serum CEA in patients with ductal carcinoma ± SD (ng/ml) (n = 126) | Mean value of serum CEA in patients with lobular carcinoma ± SD (ng/ml) (n = 08) | P value |
| 10.23±2.58 | 9.65±3.84 | 0.55 |
Table 4 shows the comparison of the level of serum CEA between the axillary lymphnode-positive and -negative cases. Out of 134 patients who were included in the study, there were 97 patients proven as axillary lymphnode positive and 37 patients as negative. Mean ± SD value of serum CEA in patients with positive axillary lymphnode was 11.73 ± 2.67 ng/ml and in patients with negative lymphnode was 8.61 ± 2.01 ng/ml (P < 0.001).

Table 5 shows the comparison of the level of serum CEA between the premenopausal and the postmenopausal breast cancer patients. Out of 134 patients who were included in the study, 53 patients were premenopausal and 81 patients were postmenopausal. Mean ± SD value of serum CEA in premenopausal patients was 10.14 ± 2.54 ng/ml and in postmenopausal patients was 10.05 ± 3.35 ng/ml (P value 0.86).

**DISCUSSION**

CEA is one of the oncofetal antigens that is produced by the normal fetal cells and can be produced in appreciable amounts by some malignant, but not normal adult cells. The presence of such antigens is thought to be associated with behavior common to both fetal and malignant cells, enabling them to grow rapidly, spread, and escape destruction by the response of host tissue. Since its discovery, CEA has been evaluated in a wide range of malignancies, including breast cancer, and historically, it has been considered the standard to which new serum markers are compared. Several studies have reported that positive serum CEA levels at the time of primary breast cancer diagnosis may represent a negative prognostic parameter.[10] Although multiple serum-based tumor markers have been described for breast cancer, such as CA 15-3, CA 27.29, tissue polypeptide antigen CEA, tissue polypeptide specific antigen, and HER2, the most widely used markers are CA 15-3 and CEA.[11]

In the present study, we made four observations. First, there was a significant difference in the levels of serum CEA before (10.71 ± 2.79 ng/ml) and after (9.73 ± 3.00 ng/ml) resection, and a further significant decline after a course of chemo-radiotherapy (7.30 ± 2.79 ng/ml). Second, there was no significant difference in the levels of serum CEA between different histological types of breast cancer (ductal 10.23 ± 2.58 ng/ml, lobular carcinoma 9.65 ± 3.84 ng/ml). Third, there was a significant difference in the levels of serum CEA between axillary lymphnode-positive (11.73 ± 2.67 ng/ml) and axillary lymphnode-negative patients (8.61 ± 2.01 ng/ml). Fourth, there was no significant difference in the levels of serum CEA between premenopausal (10.14 ± 2.54 ng/ml) and postmenopausal patients (10.05 ± 3.35 ng/ml).

Our study is supported by other studies also. Ebeling et al. reported in their study a decline in the level of serum CEA after resection of tumor in breast cancer patients.[8] Behrami et al. have also reported a decrease in the level of serum CEA after surgery and a further decline after chemo-radiotherapy.[9] They also reported increase in CEA levels in case of recurrence of the disease and metastases. Pathak et al. observed that following successful treatment, serum CEA levels fell significantly below pre-treatment level.[10] Duffy et al. found potential use of serum CEA in early diagnosis of breast cancer, determining its prognosis, prospectively predicting response and resistance to specific therapies, surveillance after primary surgery, and monitoring therapy in patients with primary disease.[11] Kiang et al. studied the tumor markers CEA and CA 15-3. Tumor marker levels in blood were studied after initiation of chemotherapy and an increase in levels was found due to tumor progression and a decrease in levels due to tumor cytolsis. They concluded the effective use of these tumor markers in monitoring the disease course and in early prediction of therapeutic response.[12] van Dalen et al. found paradoxical patterns in some patients, i.e. rise in the level of CEA at the time of tumor regression and fall in the level at the time of tumor progression.[13] This has been explained by the fact that dying cells may release a large amount of marker in the blood and the chemotherapeutic agent inhibits the release of CEA from the cell, though there is no inhibition of its synthesis.

Walker demonstrated in his study that serum CEA is related to good histological differentiation of breast cancer but not to the histological type of breast cancer.[14] Agrawal et al. also found in their study that there was no significant correlation of serum CEA to the histological type of breast cancer. In our study, there were 126 patients with infiltrating ductal carcinoma and 8 patients with infiltrating lobular carcinoma. Similar results were found in our study and there was no correlation of the histological type of breast cancer with the serum CEA.[15]
In our study, out of 134 cases, 97 patients were histologically axillary lymphnode positive and 37 were node negative. Serum CEA values in node-negative cases were significantly higher than in node-negative cases. Ghaffari et al. reported that serum CEA is the preferred marker for the detection of metastases in axillary lymphnodes.\[16\] Kuhajda et al. also found a strong relationship between elevated CEA in tumors more than 3 cm which were associated with axillary metastasis.\[17\] Bruce et al. found elevated plasma CEA in a small percentage of patients with early breast cancer and in about 60% cases with the disease disseminated to regional lymph nodes.\[18\] Similar findings were reported by Pathak et al., where serum CEA levels differed significantly with nodal status (P < 0.002) and the number involved nodes; also, patients with distant metastasis had significant rise in serum CEA levels.\[19\]

Forteva et al. found no significant relationship of serum CEA in patients with breast cancer with the menopausal status of the patient.\[19\] Luqmani et al. also obtained similar results and there was no significant relationship of serum CEA with the menopausal status of the patients with breast cancer.\[20\] Similar studies were also reported by Molina et al.\[21\] In our study, 53 patients with breast cancer were premenopausal and 81 patients were postmenopausal, and the menopausal status was not significantly related to the serum CEA values.

According to some studies, serum CEA is more sensitive as a tumor marker in breast cancer when used in combination with CA 15-3 than when used alone.\[22,23\]

CONCLUSION

Serum CEA is a tumor marker of breast cancer. The levels of serum CEA decrease after surgery and a further decrease is found after chemo-radiotherapy. The levels of serum CEA are higher in axillary lymphnode-negative patients as compared to lymphnode-negative cases. Serum CEA values were not found to have significant correlation with the histological subtype and menopausal status of the patient.

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