

# EVALUATION OF CARCINOEMBRIONIC ANTIGEN CEA AND CA15.3 TUMOR MARKERS IN PATIENTS OPERATED FOR BREAST CANCER

Mohammad Hossein Sarmast Shooshtary<sup>1</sup>, AH Talaizadeh<sup>2</sup>, S Assar<sup>3</sup>,  
B Khalaj Arnineh<sup>4</sup>, J Nateghi<sup>5</sup>, M Rahdar<sup>6</sup>

## ABSTRACT

**Introduction:** Tumor markers are biochemical signs of tumor existence and consist of cell surface antibodies, cytoplasm proteins, enzymes and hormones.

**Patients and Method:** We evaluated the variability of tumor marker levels in following-up patients without the evidence of the disease after the resection of a primary breast cancer. Carcinoembryonic antigen (CEA) and CA 15.3 were measured by commercially available methods in serial blood samples collected from 94 patients referred to surgical and oncological center of Ahwaz.

**Results:** In 72 cases with normal CA 15.3, metastasis and recurrence occurred for 12% and 4.17% respectively. In 12 cases with abnormal CA15.3 metastasis and recurrence occurred for 54.55% and 4.55% respectively. In 80 cases with normal CEA metastasis and recurrence occurred for 15% and 5% respectively, and in 14 cases with abnormal CEA metastasis and recurrence occurred for 64.24% and 14% respectively.

**Conclusion:** The incidence of metastasis is high in patients with abnormal tumor markers, and CA15.3 is more sensitive in following-up and evaluating the patient's response to the treatment.

**KEYWORDS:** Tumor marker, Breast cancer, Follow-up, Recurrence, Metastasis.

Pak J Med Sci January - March 2007 Vol. 23 No. 1 115-118

1. Dr. Mohammad Hossein Sarmast Shooshtary
  2. Dr. AH Talaizadeh  
General Surgeon,  
Department of Surgery,  
Imam Khomeini Hospital
  3. Dr. S. Assar
  4. Dr. B Khalaj Arnineh  
General Practitioner
  5. Dr. J Nateghi  
Hematologist Oncologist,  
Department of Haematology Oncology,  
Shafa Hospital
  6. Dr. M Rahdar  
Department of Mycoparasitology
- 1-6: School of Medicine,  
Jundi-Shapour University of Medical Sciences,  
Ahwaz - Iran.

Correspondences:

Dr. Mohammad Hossein Sarmast Shooshtary,  
General Surgery Ward,  
Imam Khomeini Hospital,  
Azadegan Street,  
Ahwaz - Iran.  
E-Mail: sarmastm@hotmail.com

\* Received for Publication: February 4, 2006

\* Accepted: June 14, 2006

## INTRODUCTION

Carcinoembryonic antigen (CEA) and CA15.3 are used to follow-up the breast cancer.<sup>1-7</sup> These tests are not usually used to monitor a primary cancer diagnosis;<sup>7,8</sup> nor to get to an early diagnosis of recurrence and metastasis.<sup>1,2,6,7</sup> For this purpose CA15.3 is more sensitive for early diagnosis of metastasis.<sup>6,7</sup> This prospective study was done for determination of tumor markers CEA and CA15.3 in 94 patients with breast cancer who were referred to the Ahwaz Surgery and Oncology Centers between 1997-1998.

## PATIENTS AND METHOD

Ninety-four patients with breast cancer were chosen randomly from among those who were referred to surgical and oncological centers in Ahwaz from 1997 to 1998. After surgical treatments, no clinical or paraclinical (bone scan,

chest x-ray, and sonography) evidence was detected. Following-up the signs of recurrence and metastasis was based on the clinical evidence and monthly serum level control for tumor markers CEA and CA15.3. The first sample was obtained before or early after operation. The level of CEA below or equal to 5ng and the level of CA15.3 below or equal to 30u/ml was considered normal. Patients were divided into normal and abnormal groups.

## RESULTS

The average level of CEA before treatments was 2.42 ( $\pm 0.39$ ), and after treatments was 2.43 ( $\pm 39\%$ ). The average level of CA15.3 before treatments was 25.51( $\pm 3.87$ ) and after treatments (surgery and chemotherapy) 10-61( $\pm 2.15$ ). In 72 cases with abnormal CA15.3 metastasis occurred in 54.55% and recurrence occurred in 4.55%. In 22 cases with normal CA15.3 metastasis occurred in 12% and recurrence was detected in 4.17%. In 14 cases with abnormal CEA metastasis recurrence occurred in 64.24% and 14%, respectively. In 80% cases with normal CEA metastasis recurrence occurred in 15% and 5%, respectively.

In general, patients with normal levels of both tumor markers an elevation of CA15.3 occurred in 55.56% from metastasis and for 66.67% from recurrence 2.4( $\pm 1.2$ ) months before the clinical sign of metastasis, and 2.6 ( $\pm 1.2$ ) months before the clinically evidence of recurrence. Moreover, in these groups with normal levels of tumor markers the elevation of CEA appears in 50% of patients 2.2 $\pm$ 1.1 months before the clinical signs of metastasis and 2.1 $\pm$ 1.05 months before the clinical signs of recurrence.

## DISCUSSION

Breast cancer has a major impact on the health of women.<sup>10</sup> Breast cancer is the most common female- related cancer that leads to death in mostly 40-45 year old women.<sup>9</sup> The, age-adjusted incidence of the new case has

been steadily increasing since the middle of 1940s. In the 1970s the probability of woman in the United States developing breast cancer was estimated at one in 13 in 1980 it was 1 in 11, and in 1996 the frequency was 1 in 8.<sup>9</sup>

Women with the history of invasive breast cancer are at risk developing metastatic disease, most recurrences are detected within 5-10 years after the diagnosis, but late recurrences can also occur.<sup>11</sup> As screening programs identify more patients with earlier stage disease, and as the number of women diagnosed with insitu ductal carcinoma continuously rises, there will be even more women living with a personal history of breast cancer.<sup>10</sup> On the other hand all patients who have experienced recurrence or metastasis are not considered at the end stage<sup>10</sup> and although the median survival of women with metastatic breast cancer is in the range of two to three years, but there is a great variability. Indeed, a small number of patients with metastatic disease who receive a course of chemotherapy remain relapse-free for a decade or longer.<sup>12</sup>

Although tumor markers are known as indexes for managing and following-up of the breast cancer,<sup>1,2,6,7,9,11,13,14</sup> two points are still being debated i.e. their cost effectiveness has been neither demonstrated nor disapproved; and their reliability of the currently used dichotomous division into positive/ negative cut-off should be definitely valid.<sup>4</sup>

Several studies have been done to define the sensitivity of these tests to detect recurrence and metastasis. The monoclonal antibodies CA15.3 were developed against the two antigens 115 D8 of human milk Fat globule membrane and DF3 of breast cancer.<sup>5</sup> A level below or equal to 30u/ml is considered normal. CEA is an oncofetal antigen that was first described by Gold and Freedman in 1965.<sup>15</sup> The normal level of CEA is below 5ng/ml. CEA may modestly be elevated in about 19% of smokers who don't have cancer and in 3% of the normal population. These false elevations, however, are almost always less than 10ng/ml and remain stable during serial testings, in contrast to CEA produced by recurrent tumor.<sup>15,16</sup>

In the end we conclude that 1) Patients with abnormal CA15.3 had a higher rate of metastasis compared with those who had normal CA15.3, but this was not true about recurrence, 2) patients with abnormal CEA had a higher rate of recurrence and metastasis. According to these findings it appears that the two tumor markers CEA and CA15.3 have valuable prognostic indicators in following-up of breast cancer. Pathak and cooperators reported<sup>1</sup> that serum level of CEA is a prognostic indicator for the advanced breast cancer and serial serum CEA levels could predict metastasis 3.9 months before the clinical evidence is advanced. Bottini also concluded pretreatment elevated CA15-3 levels correlated with a higher recurrence rate, further supporting the prognostic significance of this tumor marker.<sup>2</sup> According to the serum levels of CEA and CA15.3 compared and the clinical status, CA15.3 was more sensitive and specific in metastatic breast cancer than CEA.<sup>6,7</sup> These findings support our results.

It is also discovered in this study that CA15.3 compared with CEA was more sensitive in detecting the disease earlier before the clinical evidence of the disease. We also conclude that treatment (surgery and chemotherapy) results is more reducing in CA15.3 than CEA level, which coincides more with the response to the treatment.

We recommend that serial levels of CA15.3 be controlled in all patients with a normal and an abnormal level of CA15.3 after the primary diagnosis for early detection of recurrent and metastatic disease, and CEA be checked in patients with abnormal level of CEA for early diagnosis of recurrent disease.

One of the other tumor markers described for breast cancer is CA125. Increased CA125 was associated with metastasis in or near the pleura, and in the stage IV of breast cancer it was related to poor prognosis.<sup>14</sup>

One of the important point of cancer diseases is that tumor markers are not usually used for screening because of unreliability, in one study it was appeared that CEA serum levels

increased in only 20% of primary cancers, although this means poor prognosis.<sup>11</sup>

Monthly breast self examination, annual mammography of the preserved and contralateral breast, gynecologic examination, and any other tests like tumor markers, bone scan and sonography should not replace conventional classic managements.<sup>10,17-19</sup>

## REFERENCES

1. Pathak KA, Khanna R, Khanna HD, Khama S, Gupta S, Khanna NN. Carcinoembryonic antigen: An invaluable marker for advanced breast cancer. *J Postgrad Med* 1996;42(3):68-71.
2. Bottini A, Berruti A, Tampellini M, Morrica B, Brunelli A, Gnocchi E. Influence of neoadjuvant chemotherapy on serum tumor markers CA15-3, MCA, CEA, TPS and TPA in breast cancer patient with operable disease. *Tumour Biol* 1997;18(5):301-10.
3. Gion M, Peloso L, Mione R, Vignati G, Fortunato A, Saracchini S. Tumor markers in breast cancer monitoring should be scheduled according to initial stage and follow-up time: A prospective study on 859 patients. *Cancer J* 2001;7(3):181-90.
4. Gion M, Barioli P, Mione R, Cappelli G, Vignati G, Fortunato A, et al. Tumor markers in breast cancer follow-up: A potentially useful parameter still awaiting definitive assessment. *Ann Oncol* 1995;6 suppl:31-5.
5. Gion M, Cappelli G, Mion R, Pistorello M, Meo S, Vignati G. Evaluation of critical differences of CEA and CA 15-3 levels in serial samples from patients operated for breast cancer. *Int J Biol Marker* 1994;9(3):135-9.
6. Hou MF, Huang TI, Hsieh JS, Huang YS, Huang CJ, Chan HM, et al. Comparison of serum CA15-3 and CEA in breast cancer. *Gaoxiong Yi Xue Ke Xue Za Zhi* 1995;11.
7. Arsalan N, Serdar M, Devci S, Ozturk B, Narin Y, Igan S. Use of CA15-3, CEA and prolactin for the primary diagnosis of breast cancer and correlation with the prognostic factors at the time of initial diagnosis. *Ann Nucl Med* 2000;14(5):395-9.
8. Abertini, Paul M, Sondel MR. Tumor immunology and immunotherapy. In: Martin D. Ahloff, James O. Anitage, Allen S. Lichter, John E. Njederhumber. *Clinical oncology*. Second edition. Churchill Livingstone 2000;214-37.
9. Bland KI, Beenken SW, Copeland EM. The breast. In: Brunicardi FC, Anderson DK, Billjar TR, Dunn DL, Hunter JG, Pollock RE: *Schwartz principles of surgery* Eight edition, 2005;pp 453-496.
10. Winer EP, Morro WM, Kent OC, Harris JR. Malignant tumors of the breast. In: Vincent T. Devita, Jr. Samuel Hellman, Steven A. Rosenberg. *Cancer principles and practice of oncology* 6<sup>TH</sup> Edition 2001;2:pp1651,1698-9.

11. Saphner T, Turmeyer DC, Gray R. Annual hazard rate of recurrence for breast cancer after primary therapy. *J Clin Oncol* 1996;14:2738.
12. Greenberg PAC, Hortobagyi GN, Smith TL. Long-term follow-up of patients with complete remission following combination chemotherapy for metastatic breast cancer. *J Clin Oncol* 1996;14:2197.
13. Meyers WC, Chari RS, Schaffer BK, Darling CE, Yang POS. In: Neoplasms. Courtney M. Townsend Jr, Harris JW. Sabiston text book of surgery. Sixteenth edition, W.B. Saunders company 2001;Vol.3:pp1029- 30.
14. Nortum LF, Erikstein B, Nustad K. Elevated CA15-3 in breast cancer- Assign of advanced disease. *Tumor Biol* 2001;22(4):223-8.
15. Gold P, Freedman S. Demonstration of tumor-specific antigens in human colonic carcinomata by immunological tolerance and absorption techniques. *J Exp Med* 1995;121:439.
16. Alexander JC, Silverman NA, Chretien PB. Effect of age and cigarette smoking on carcinoembryonic antigen levels. *JAMA* 1975;235.
17. Mitchell EP: Role of carcinoembryonic antigen in management of advanced colorectal cancer. *Semin Oncol* 1998;25:12.
18. Sauer H. Significance of tumor markers during the follow-up of women without. Symptoms after treatment of primary breast cancer. *Anticancer Res* 1997;17(4B):3059-61.
19. Recommended Breast Cancer Surveillance Guidelines Adopted on February 20, 1997 by American Society of Clinical Oncology.