Breast Cancer: Current Research

Osman et al., Breast Can Curr Res 2016, 1:4

Research Article OMICS International

High Concentration of Tumor Marker Cancer Antigen CA15-3 in Breast Cancer Patients after Surgery

Adam MA Osman[1], **Mohamed E Hamid**[2], **Ayda H Satti**[3] **and Ibtisam A Goreish**[4]

[1]*Department of Animal Resource, Ministry of Agriculture, Kingdom of Saudi Arabia, Abha, Saudi Arabia*

[2]*Department of Clinical Microbiology and Parasitology, College of Medicine, King Khalid University, Box 641, Abha 61314, Saudi Arabia*

[3]*Department of Surgery, Khartoum Teaching Hospital, Khartoum, Sudan*

[4]*Director General of Animal Resources Research Corporation, Khartoum, Sudan*

***Corresponding author:** Adam MA Osman, Department of Animal Resource, Ministry of Agriculture, Kingdom of Saudi Arabia, Abha, Saudi Arabia, Tel: 00966550979809; E-mail: mohammedai41@yahoo.com

Received date: Oct 20, 2016; **Accepted date:** Nov 08, 2016; **Published date:** Nov 14, 2016

Abstract

Background: Cancer antigen15-3 (CA15-3) is the most common tumor marker in breast cancer patients. The aim of the study analysis was to investigate the correlation, if there is any, of the levels of CA15-3 in patients with breast cancer and healthy females and to evaluate the efficacy of cancer associated antigen 15-3 (CA15-3) in monitoring breast cancer.

Methods: Clinical assessment was carried out in 40 serum samples. Female patient (n=20) were histologically verified of having breast cancer after chemical treatment and surgery. Healthy females subjects (n=20) with no history of breast cancer were included as controls. Enzyme linked immunosorbent assays was used for the quantitative determination of the cancer associate antigen.

Result: Elevation of CA15-3 levels was found associated with breast cancer patients. The serological levels were found around 75.04 ± SD/ mL (P=0.001), whereas the level among the control group was 13.99 ± SD/ mL).

Conclusion: CA15-3 concentration levels were found elevated in breast cancer patients with significant level demonstrating its diagnostic routine use.

Keywords: Breast cancer; Metastasis; Tumor; Chemotheray; Blood sample

Introduction

Breast cancer is a malignant (cancerous) growth begins in the tissues of the breast and the most common cancer in women, but it can also appear in men. Breast cancer is stage-biological process causing multiple genetic and epigenetic changes in the epithelial cells of the breast over a period of several years. The biological progression of breast cancer is based on the inability of differentiation, loss of contact inhibition, uncontrolled growth, the ability to migrate, invasion, angiogenesis metastasis, and the ability to avoid immune control of tumor cells.

Breast cancer tumor cells generally retain the morphological and functional characteristics of normal tissue cells [1]. In Sudan, breast cancer and cervical cancer account for about 50% in women. Routine screening for these cancers has markedly reduced the mortality in the developed world, but in developing countries, which largely lack screening programs; these two cancers remain the primary cause of death [2]. Serum tumor markers have been widely used as non-invasive tools for measuring treatment response, early diagnosis of recurrence and predicting prognosis. In breast cancer, the most widely used serum tumor markers are cancer antigen 15-3 (CA 15-3) and carcinoembryonic antigen (CEA). The American Society of Clinical Oncology guidelines state that there is insufficient data to recommend the use of serum tumor marker although the marker is able to detect the recurrence of disease before clinical or diagnostic imaging modalities [3].

CA 15-3 and CEA are the markers most widely used for surveillance purposes and monitoring of treatment response in clinical practice [4]. Cancer antigen 15-3, or CA15-3, is an epitope of a large transmembrane glycoprotein named MUC1 that is derived from the MUCI gene. The MUCI protein, also known as polymorphic epithelial mucin or epithelial membrane antigen, has a large extracellular region, a transmembrane sequence, and a cytosolic domain. This protein is frequently overexpressed and aberrantly glycosylated on its extracellular region in breast cancer. CA 15-3 is a glycoprotein with a molecular weight of 300-450 kDa. It is elevated in breast, ovarian, pancreatic, lung and colorectal cancers [1].

The reference range of serum CA15-3 is less than 30 u/ml. The upper limit of the range varies depending on the laboratories and kit, methods, used for the test. Values obtained with different assay kits, methods, or laboratories cannot be used interchangeably. We focused on the breast cancer marker specific CA15-3 is useful for early diagnosis and treatment of breast cancer that can be eliminating the suffering and death due to breast cancer.

Materials and Methods

Ethical consideration

Ethical approval of the study was obtained from the ethical committee of the Sudan Academy of Sciences.

Study design

This study was a cross sectional study.

Patients

Clinical assessment was carried out in 40 female. 20 Females were histologically verified of having breast cancer at different stages after receiving chemical treatment and surgery. Patients were in the age group of 18-70 years of age and were examined over a period from April 2013 through January 2016 at the Brest Clinic at (Khartoum Technical Hospital and Al Amal Hospital).

All Breast cancer patients were staged according to standard criteria based on data of (TNM) concerning age, type of surgery, clinical pathology such as tumor size, lymph node status and histological such as Metastases and Union for International Cancer Control (UICC) [5]. Data for each patient were collected through clinical charts. The control group consisted of 20 healthy females subjects with no history of breast cancer age group 25-45 years. Blood samples were collected from patients and healthy controls in 10 ml glass tubes without additive; serum was separated by centrifugation (2500 rpm 10 min) and stored at 20°C for analysis.

Assays

Serum CA15-3 was measured by the commercially available CanAg CA15-3 EIA kits (Fujirebio Diagnostics, Inc.). Kits were used for the quantitative determination of the cancer associated antigens in serum. The markers (CA15-3) were analyzed by direct sandwich technique by two monoclonal antibodies. When the reaction was terminated by a stop solution (0.12 M hydrochloric acid), the absorbance (optical density at 405-630 nm) was measured by ELISA reader. The standard curve was prepared based on absorbance and the established cut-off was 30 U/ml [6].

Statistical analysis

Statistical analysis was performed by T Test Paired Samples Test with 95% confidence intervals were used to convey the effects and calculate the correlation. The P value of <0.05 was considered as significant.

Results

Our study examined 40 females, of these 20 serum samples were from patients histologically confirmed breast cancer. The mean age was 44 years (range 18-70). And 20 serum samples from healthy subjects with no history of breast cancer the men age was 35 years (range 25-45, Cancer antigen (CA15-3) tumor marker concentrations ware significantly higher in patients with breast cancer (Table 1). The serological levels of CA15-3 was (75.0350 ± 15.12885 U/ml) in breast cancer patients (P=0.001). The serum levels in normal controls was (13.8950 ± 46155 U/ml). The 95% confidence interval of the differences was 92.92 (P=0.001) when T Test paired samples statistics was used. There was no statistically difference between serum levels of (CA15-3) and the clinicopathological characteristics stage of tumor, nodal status, age, histology and tumor size. Elevation of CA15-3 levels ware only correlated with breast cancer patients (P=0.001).

Characteristic	N	%
Age		
Less or equal to 50	15	75
Greater of equal to 50	5	25
Histology		
Invasive ductal carcinoma (IDC)	9	45
Lobular infiltrating carcinoma (LIC)	3	15
Metastasis (M)	8	40
Surgery		
Mastectomy	11	55
Partial mastectomy	6	30
Unknown	3	15
Site of cancer		
Left	10	50
Right	10	50
Grade of tumor		
High	13	65
Low	7	35
Stage of tumor		
I and IIA	12	60
IIB,III and,IV	8	40
Tumor size (cm)		
Less or equal 2	7	35
Grade than 2	13	65
Nodal status		
Negative	9	45
Positive	11	55

Table 1: Main clinical pathological characteristics of breast cancer patients.

Discussions

Tumor marker detectable in serum would be helpful to contribute to the early diagnosis, provided that the test is sensitive and specific enough to already of the disease concerned. Specific serum tumor marker tests at all stages of disease is needed independently to evaluate the condition of the patient. Tumor marker determinations in serum could also be used as prognostic factors to predict impending relapse following primary treatment, or as a reason for starting adjuvant or palliative therapy. The tumor marker CA15-3 are widely used for the

early diagnosis of breast cancer. In our study the elevation of CA15-3 serological levels was detected in breast cancer patients. This agrees with the study of the relationship between preoperative serum CA15-3, CEA Levels and Clinicopathological parameters in breast cancer [6]. Our finding was similar to the result of Daniel et al. [5]. We found that the mean serum CA 15-3 levels in patients before surgery were significantly higher (36.59 U/ml) compared with those of CA 15-3 after surgery (27.11 U/ml). We also found that elevated preoperative serum levels of CA 15-3 were highly correlated with the presence of metastatic disease. In particular, among 305/700 patients (43, 6%) that displayed over cut-off (>40 U/ml) preoperative levels of CA 15-3, 94 patients (30, 8%) developed advanced disease (metastases to distant sites). By contrast, in a subgroup of 395/700 patients (56.4%) with CA 15.3 serum levels<40 U/ml, only 32/305 patients (8%) showed signs of advanced disease during follow-up. Cox regression analysis revealed that only the presence of metastasis and the increased serum levels of CA 15-3 after surgery are significant risk factors for relapse of disease. The study by Duffy et al. [7] which included 600 patients with histological confirmed breast cancer investigated the concentration of CA15-3. The result of CA15-3 was significantly higher concentration. The sensitivity of CA 15-3, CEA and serum HER2 in the early detection of recurrence of breast cancer by Pedersen et al. [8] agreed with our result of elevated serum levels of CA15-3 in the group of patients with distant metastasis disease.

Conclusions

In conclusion, our result shows that the tumor marker cancer antigen (CA15-3) concentration levels were found highly significant and elevated in breast cancer patients. We recommended that serum tumor marker CA15-3 is useful for management of patients with breast cancer. However it may be useful as prognostic tumor marker to monitoring treatment and for early diagnosis of breast cancer [9-21].

Acknowledgments

We thank to the staff of Institute of Endemic Disease University of Khartoum, especially Dr Muzamil Mahdi Head Department of Parasitology and Medical Entomology, Mr Musab Mohamed Ali Department of Parasitology and Molecular Biology East Nile University and Dr Mohamed Osman Head Department of immunology lab at central lab Khartoum Sudan.

References

1. Fejzic H, Mujagic S, Azabagic S, Burina M (2015) Tumor marker CA15-3 in breast cancer patients. Acta Med Academica 44: 39-46.
2. Hamad HMA (2006) Cancer initiatives in Sudan. Annals of Oncol 17: 32-36.
3. Guadagni F, Ferroni P, Carlini S, Mariotti S, Spila A (2001) A Re-Evaluation of Carcinoembryonic Antigen(CEA) as a Serum Marker for Breast Cancer: A Prospective Longitudinal Study. Clinic Cancer Res 7: 2357-2362.
4. Geng B, Liag MM, Ye XB, Zhao WY (2015) Association of CA15-3 and CEA with clinicopathologcal parameters in patients with metastatic breast cancer. Molecular and Clinical Oncol 3: 232-236.
5. Daniele A, Divella R, Trerotoli P, Elena M (2013) Clinical usefulness of cancer antigen 15-3 in breast cancer patients before and after surgery. The Open Breast Can Jl 5: 1-6.
6. Moazzezy N, Farahany TZ, Oloomi M, Bouzari S (2014) Relationship between preoperative serum CA15-3 and CEA levels and clinicopathological parameters in breast cancer. Asian Pacific J of Cancer Prevention 15: 1685-1688.
7. Duffy MJ, Duggan C, Keane R, Hill ADK, McDermott E, et al. (2004) High preoperative CA15-3 concentrations predict adverse outcome in node-negative and node-positive breast cancer. Clinic Chem 50: 3559-3563.
8. Pedersen AC, Srensen PD, Jacobsen EH, Madsen JS, Brandslund I (2013) Sensitivity of CA15-3, CA and serum HER2 in the early detection of recurrence of breast cancer. Clin Chem Lab Med 51: 1511-1519.
9. AVerring A, Clouth P, Ziolkowski, Oremek GM (2011) Clinical usefulness of cancer marker in primary breast cancer. International Scholarly Research Network ISRN Pathology.
10. Berruti A, Tampellini M, Torta M, Buniva T, Gorzegno G, et al. (1994) Prognostic value in predicting overall survival of two mucinous markers CA15-3 and CA125 in breast cancer patients at first relapse of disease. Eur J Cancer 30: 2082-2084.
11. Colomer R, Ruibal A, Genolla J, Rubio D, Delcampo JM, et al. (1989) Circulating CA15-3 levels in the postsurgical follow-up of breast cancer patients and in non-malignant disease. Breast Cancer Res Treat 1: 123-33.
12. Lassig D, Nagel D, Heinemann V, Untch M (2007) Anticancer Res 27: 1963-1968.
13. Duffy MJ (1999) CA15.3 and related mucins as circulating markers in breast cancer. Ann Clin Biochem 36: 579-86.
14. Kumar JK, Aronsson AC, Pilko G, Zupan M, Kumar K, et al. (2016) A clinical evaluation of the TK210 elisa in sera from breast cancer patients demonstrates high sensitivity and specificity in all stages of disease. Tumor Biol.
15. Jaeger W, Eibner K, Loffler B, Gleixner S, Kramer S (2000) Seral CEA and CA15-3 measurement during follow-up of breast cancer patients. Anticancer Res 20: 5179-5182.
16. Thriveni K, Krishnamoorthy L, Ramaswamy G (2007) Correlation study of carcino embryonic antigen &cancer antigen 15-3 in pretreated female breast cancer patients. Indian Jl of Clinical Biochem 22: 57-60.
17. Keyhani M, Nasizadeh S, Dehghannejad A (2005) Serum CA15-3 measurements in breast cancer patient before and after mastectomy. Arch Iranian Med 4: 263-266.
18. Martoni A, Zamagni C, Bellanova B (1995) CEA, MCA, CA15.3 and CA 549 and their combinations in expressing and monitoring metastatic breast cancer: a prospective comparative study. Eur J Cancer 31: 1615-21.
19. Moazzezy N, Farahany TZ, Oloomi M, Bouzari S (2014) Relationship between preoperative serum CA15-3 and CEA levels and clinicopathological parameters in breast cancer. Asian Pacific Jl of Canc Prevention 15: 1685-1688.
20. Safi F, Kohler I, Rottinger E, Beger H (1991) The value of the tumor marker CA15-3 in diagnosing and monitoring breast cancer. A comparative study with carcinoembryonic antigen. Cancer 68: 574-582.
21. Vrdoljak D, Knezevic F, Ramljak V (2006) The relation between tumor marker CA15-3 and metastasis in interpectoral lymph nodes in breast cancer patients. Saudi Med J 27: 460-462.