DETERMINATION OF CANCER ANTIGEN CA15-3 AND ALPHA FETO PROTEIN (AFP) LEVELS AS TUMOR MARKER IN PATIENTS WITH BREAST AND PROSTATE CANCER

Rana Kareem Al- Saady[a] and Salah Mohammed Fizea[a]*

Keywords: CA15-3, AFP, breast cancer, prostate cancer.

The objective of the present study is to evaluate the values of cancer antigen (CA15-3) and alpha feto protein (AFP) in patients with breast and prostate cancer. The results revealed the values for CA 15-3 in serum of G1 showed a highly significant increase compared to normal healthy subjects, but CA15-3 in serum of G2 was compatible with control. The results showed the value of serum AFP in G1 (was not significant different) when compared to control, while a highly significant difference in G2 was noticed when compared to healthy subjects.

*Corresponding Authors
E-Mail: salahmf79@yahoo.com
[a] Department of Chemistry, College of Education for Pure Science, Ibn Al-Haitham, University of Baghdad

Introduction

Tumor markers are biochemical substances elaborated by tumor cells either due to the cause or effect of malignant process. A tumor marker produced by the tumor and, when present in significant amounts, indicates the presence of a cancer.[1, 2]

Cancer antigen CA15-3 is heterogeneous 300 KD glycoprotein antigen was defined by using two monoclonal antibodies 115D8 and DF3 raised against breast carcinoma cells. The diagnostic sensitivity of the CA15-3 for breast carcinoma is low as its elevated levels are also observed in benign breast diseases and in liver cirrhosis, acute and chronic hepatitis. The marker concentration is also elevated in metastatic cancers of pancreas, ovary, colorectal, lung, stomach, and uterus.[3,4]

Alpha feto protein (AFP), a very popular and extensively studied carcino embryonic glycoprotein/oncofetal antigen, is a major fetal serum globulin with a molecular weight of approximately 65,000 D. The single chain glycoprotein has carbohydrate content of 3 % and amino acid sequence similar to that of albumin. It is expressed either during malignancy or during intra uterine or early postnatal life.[5,6] An increase in serum AFP concentration below 400 ng mL^{-1} was also reported in 10-15 % of cases of acute and chronic hepatitis, liver cirrhosis and secondary hepatic malignancies.[7,8]

Experimental part

The study was carried out on 71 subjects comprising of 36 patients with breast cancer G1, 10 patients with prostate cancer G2, and 25 normal healthy controls with range of (40-55) years. The patients were admitted to Al Khadmiya Teaching Hospital for treatment.

Blood sample 3 mL were collected left at room temperature for 15 min centrifuged at (3000 rpm). Serum was separated and freezed until time of analysis.

Serum CA 15-3 determination

Serum CA15-3 was estimated using a kit (DrG, Germany), the analysis based on the principle of a solid phase enzyme linked immunosorbent assay (ELISA).[9,10] The concentration of CA15-3 was evaluated from standard curve drawn between standards of CA15-3 provided with the kit and absorbance at 450 nm.

Serum AFP determination

Serum AFP was estimated using a kit (BioCheck, USA), the analysis based on the principle of a solid phase enzyme linked immunosorbent assay (ELISA)[11]. the concentration of AFP was evaluated from standard curve drawn between standards of AFP provided with the kit and absorbance at 450 nm.

Statistical Analysis

The results were expressed as mean±SD of mean, using Statistical Package for Social Sciences (SPSS) version 19.0 and Microsoft Excel 2010 for data processing and graph construction. Statistical significant difference was ($p \leq 0.05$) .and highly significant difference was ($p \leq 0.001$).

Results and Discussion

The values of serum CA15-3 and AFP of breast cancer G1 , prostate cancer G2 and healthy subjects G3 are shown in Table 1.

Table 1. Value mean±SD for CA15-3 and AFP in all studied groups.

Group	CA15-3 U mL^{-1}	*P*	AFP ng mL^{-1}	*P*
Control *N*=25	18.18 ±4.42		3.98±1.20	
G1 *N*=36	52.65 ±10.37	≤0.001	4.59±1.05	>0.05
G2 *N*=10	20.25 ±1.68	>0.05	8.43±0.59	≤0.001

CA 15-3 in serum of G1 showed a significant increase compared to normal healthy subjects, but CA15-3 in serum of G2 was compatible with control.

Recent study suggest that a very slight increase in CA15-3 of breast cancer in few patients indicating a chance of disease progression or recurrence.[12] CA15-3 serum levels are influenced by disease extent.[13] Another study also reported an elevated level of CA 15-3 in metastatic condition.[14] Elevated CA15-3 levels are more common in metastatic breast cancer patients than with other tumor markers.[15]

The role of tumor markers in the management of breast cancer patients is limited to patients with advanced disease, This is because that they are rare abnormal in early disease or with local recurrence. Thus tumor marker analysis is appropriate in previously diagnosed patients at high risk for recurrence to detect early disease dissemination and in patients with metastatic disease to evaluate therapeutic response.[14]

A recent study suggested that serum tumor markers are abnormally elevated in patients with breast cancer. CA15-3 is useful clinical marker, good indicator of disease extent and may have important prognostic value. One of the main request for an ideal cancer marker it is suitability for preclinical screening. Therefore, prerequisite would be high sensitivity as well as specificity with respect to the detection of primary breast cancer.[16] Other study showed CA 15-3 to be one of the first circulating prognostic factors for breast cancer. Preoperative concentration thus might be combined with existing prognostic factors for predicting out come in patients with newly diagnosed breast cancer .and thus CA15-3 is the most widely used serum marker in breast cancer,[17] also other study suggested that circulating CA15-3 antigen level are elevated in more than 70 % of breast cancer patients with distant metastases.[18] CA15-3 has been found useful in monitoring the course of advanced breast cancer and in the postsurgical follow-up of patients with breast carcinoma.[19] CA- reactive antibodies 115D8 and Df3 detect individual antigen that are present in human primary epithelial carcinoma.[20] Ninety-three percent of 140 human epithelial primary tumors reacted with monoclonal antibodies 115D8 or Df3, including breast, ovarian, lung, and also colon and gastric carcinoma.[21] In general, changes in tumor markers accurately and consistently reflected changes in disease status but not in the pertinent issue, However the use of tumor markers in clinical practice will lead to more effective treatment remain controversial.CA15-3 is a marker of distant metastasis in breast carcinoma with high specificity and moderate sensitivity.[22]

From the same table the value of serum AFP in G1 showed no significant difference when compared to control , while a highly significant difference in G2 when compared to healthy subjects was noticed.

Recent study demonstrated that AFP together with other serum markers is a well known useful clinical tool for diagnosis and follow up of patients with germ cell tumors. However many different benign and malignant clinical condition may represent serum elevation of AFP without germ cell tumor growth. Therefore all clinical conditions characterized by serum AFP increase, other than germ cell tumor, have to be taken into account before assuming that the elevation of AFP reflects the activity of this malignancy.[23] Other tumors have been associated with elevated AFP plasma levels such as pancreatic cancer (23 %), gastric cancer (20 %), bronchial cancer (7 %), colorectal cancer (5 %), and with lower frequency in cancer of the esophagus, small bowel, gallbladder, breast, endometrium, kidney, prostate and metastatic liver disease.[24]

Conclusion

A conclusion could be drawn from this study that CA15-3 elevated in breast cancer cases only, while AFP elevated in prostate cancer cases only.

References

[1]Del Villano, B. C., Brennan, S., Brock, P., *Clin. Hem*., **1983**, *29*, 549-52.

[2]Bhattacharya, S., Siegel, E. R., Petersen, G. M., Chari, S. T., Suva, L., Haun, R. S., *Neoplasia*, **2004**, *6*, 674-86.

[3]Helfrich, G., Klapdor, U., Bahlo, M., In: Klapdor, R (ed.): New tumor markers and their monoclonal antibodies – actual relevance for diagnosis and therapy of solid tumors. *4th Symp. Tumor Markers*, Hamburg **1986**, George Thieme Verlag, Stuttgart New York, **1987**, 287-90.

[4]Aabo, K., Pedersen, H., Kjaer, M., *Eur. J. Cancer Clin. Oncol.*, **1986**, *22*, 211-7.

[5]Wu, J. T., Knight, J. A., Knight, D. P., CEA in the clinical diagnosis and treatment of colorectal cancer. In: ACP Clinical Chemistry Check Sample, *III. Am. Soc. Clin. Pathol*., Chicago, 1986.

[6]Malati, T., Saraswathi, A., Vittal, P. V., Ananth Reddi, P., *Asian J. Clin. Sci*., **1988**, *8*, 33-5.

[7]Malati, T., *Clin. Proc. NIMS*, **1989**, *4*, 169-74.

[8]Wang, P. Y., *Chung-Hua Chun Liu Tsa Chih*, **1991**, *13*, 61-3.

[9]Morimoto, H., Tanigawa, N., Inoue, H., *Cancer*, **1988**, *61*, 84-8.

[10]Chittoor, S., Swain, S., *Am. Fam. Physic.*, **1991**, *44*, 453-462.

[11]Engall, E., *Methods in Enzymology*, Van Vunakis, H., and Langone, J. J.(eds), Academic Press, NewYork, **1980**, *70*, 419-492.

[12]Prabasheela, B. and Arivazhagan, R., *Int. J. Pharm. Bio Sci*., **2011**, *2(2)*, 34-38.

[13]Tampellini, M., Gorzegno, G., Sarobba, G. M., Durando, A., Arese, P., Manzen, E., Castiglione, F., Malters, A., De, Nuzzo, F., Dogliottti, L., *Eur. J. Cancer*, **1998**, *34(5)*, 105.

[14]Ann Dnistrian, A., Morton Schwartz, K., Ernest Greenbery, J., Carol Smith, A., and Delia Schwarty, C., *Clin. Chim. Acta*, **1991**, *200*, 81 – 94.

[15]James, T. W. U., In: Henry JB (eds). *Clinical Diagnosis and Management by Laboratory Methods*, 20th Edn, New York, WB Saunders, **2001**, 1028 - 1042.

[16]Verring, A., Clouth, A., Ziolkowski, P., and G. Oremek, M., *J Isr . Pathol.*, **2011**.

[17]Michael, J., Duffy, J., *Clin. Chem*., **2006**, *52(2)*, 345-351.

[18]Colomer, R., Ruibal, A., Genollk, J., & Salvador, L., *Brit. J. Cancer*, **1989**, 59, 283-286.

[19]Hayes, D. F., Zurawski, R., Kufi, W., *J. Clin. Oncol.*, **1986,** *4*, 1542.

[20]Hilkens, J., Buijs, F., Hilgers, J., *Int. J. Cancer*, **1984**, *4*, 197.

[21]Zotter, S., Hageman, P. C., Mool, J. W., Lossnitzer, A. and Hilger, J., *Cancer Res*., **1989.**

[22]Tomlinson, I. P. M., Whyman, A., Barrett, J. A., and Kremer, J. K., Eur. J. Cancer, **1995**, *3H(6)*, 899-902.

[23]Iafrate, M., Rossato, M., *J. Androl. Sci.*, **2009**, *16*, 21-24.

[24]Schefer, H., Mattmann, S., Joss, R. A., *Ann Oncol*., **1998**, *9*, 667-72.

Received: 14.05.2015.
Accepted: 07.07.2015.