EVALUATION OF SERUM ADENOSINE DEAMINASE AND 5'-NUCLEOTIDASE ACTIVITIES AS PROBABLE MARKERS IN OVARIAN CANCER

Pragathi, P., Bharath Kumar, P.V., Amar Kumar P., Ramakanth Reddy, M., Sravani, V., Neeraja, J., Reebea Mary Eapen, Gopalakrishna, K.

Department of Biochemistry, Kasturba Medical College, Manipal

ABSTRACT

Adenosine deaminase (ADA) and 5'-nucleotidase (5'-NT) activities were measured in sera of patients with ovarian cancer and patients with benign ovarian tumour. The results were compared with that of a control group consisting of healthy women. ADA levels were significantly increased ($P < 0.001$) in the ovarian cancer group ($n=50$) but not in the benign group ($n=28$) when compared to the controls ($n=20$). The results indicate that ADA and 5'-NT levels may help to differentiate malignant conditions from benign tumours of the ovary in addition to the existing tests such as serum CA-125 levels and histopathological study.

KEY WORDS

5'-NT, ADA, CA -125, Ovarian cancer.

INTRODUCTION

Changes in the levels of adenosine deaminase (ADA) and 5'-nucleotidase (5'-NT), both being the enzymes involved in nucleotide breakdown, is expected to occur in malignant conditions of any tissue. Likewise, increased ADA activity in serum and tumour tissues has been reported in cancer conditions of various tissues like skin, breast and colon (1,2,3). Similarly serum 5'-NT level is reported to be elevated in cancers of the ovary (4) and liver (5, 6).

However, the studies done regarding 5'-NT in ovarian cancer are very few (4). We could not get any report on ADA levels in ovarian cancer. Hence the present study was conducted with the objective of evaluating the usefulness of measuring serum ADA and 5'-NT levels in ovarian cancer.

MATERIALS AND METHODS

The study was carried out in the year of 2001- 2003 for a period of 16 months and the patients were selected from the population attending the Kasturba Hospital, Manipal. Our study comprised of the following three groups:

1. Ovarian cancer group: This consisted of patients with adenocarcinoma of ovary of both serous and

mucinous type as proven by histopathological report ($n=50$).

2. Benign ovarian tumour group: Consisted of cystadenoma patients ($n=28$).
3. Control group: Consisted of healthy women of different ages above 22 years ($n=20$).

Specimen

The blood samples were collected without anticoagulant before starting any treatment in the patient groups. Serum was used for the biochemical analyses.

METHODS

The biochemical tests carried out in each sample were CA-125, ADA and 5'-NT. Serum CA-125 was estimated by Microparticulated enzymatic immunoassay (MEIA) method in the AxSym analyzer of Abbott Laboratories, USA. Serum ADA was estimated by the colorimetric method of Giusti (7) in which Adenosine is used as the substrate and the ammonia liberated is measured as blue indophenol. 5'-NT was estimated by the colorimetric method of Raymond John and David Gwynne Williams (8) in which 5'-adenosine monophosphate (5'-AMP) was used as the substrate and the liberated phosphate is measured. Nickel was used to differentiate the activities of alkaline phosphatase and 5'-NT.

Chemicals

All general chemicals were of reagent grade. Adenosine was purchased from SISCO Research

Author for Correspondence :

Dr. Gopalakrishna K.
Department of Biochemistry
Kasturba Medical College, Manipal-576 104.
Telephone: 2571201, Extn.: 22402.

Laboratories, India. 5'-AMP disodium salt was purchased from E-Merck, Germany.

Statistical analysis

Statistical analysis was done using the student's 't' test. Comparisons were made between controls and the benign group, between the control group and the cancer group and also between the benign group and the cancer group. Correlation was analysed between CA 125, ADA and 5'-NT including both cancer group and benign group in the analysis.

RESULTS

The CA 125 values in serum ranged from 71-6,000 U/ml in the ovarian cancer group (Ca ovary) and 3-61 U/ml in the benign group.

There was a marked increase in ADA levels in the ovarian cancer group when compared to controls ($P < 0.001$, Table 1) and when compared to the benign group (not significant). However, there was no difference in the ADA levels in the benign group when compared to the controls. The sensitivity of ADA as a tumour marker was found to be 56% and the specificity was 78%. The cut-off value for ADA was taken as 30 U/L which is the upper limit of the range obtained for healthy controls.

The mean serum 5'-NT value was found to be elevated in ovarian cancer group when compared to both the control and the benign group (Table 1) even though there was no statistical significance. The sensitivity and specificity of 5'-NT estimation was calculated to be 38% and 86% respectively. The cut-off value for 5'-NT was taken as 18 U/L, the upper limit of the range obtained for healthy controls.

No significant correlation was observed between CA 125 and ADA and between CA 125 and 5'-NT.

DISCUSSION

The results of the present study show that both ADA and 5'-NT levels are increased only in ovarian cancer

Table 1. Serum CA 125, ADA and 5'-NT levels in different groups

GROUP	CA 125 (U/ml)	ADA (U/L)	5'-NT (U/L)
Control n=20	10.9±1.45	20.11±1.49	11.7±1.41
Benign n=28	17.5±2.90	25.3±3.10	9.2±1.67
Ovarian cancer n=50	1467±266.7**	42.94±4.23*	16.9±2.18

Values are expressed as Mean±SE.
 * $P < 0.001$ when compared to the control group.
 ** $P < 0.001$ when compared to the control and benign group.

but not in the benign group. These findings suggest that the elevated levels are certainly due to the presence of cancer cells. Hence these two parameters can serve as tumour markers and may be useful in differentiating ovarian cancer from benign tumours of the ovary, in addition to the well-established marker of ovarian cancer, CA-125. However, detailed study of ADA and 5'-NT is required considering the various stages of cancer as well as pre and post-therapeutic changes to confirm their clinical utility in the management of ovarian cancer. The statistical significance and sensitivity and specificity studies indicate that ADA is a better parameter than 5'-NT in the study of ovarian cancer.

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Table 2. Classification of patients according to the enzyme activity

	Ovarian cancer (n=50)		Benign (n=28)		Sensitivity %	Specificity %
	Enzyme activity		Enzyme activity			
	Normal	High	Normal	High		
ADA	22	28	22	6	56	78
5'-NT	31	19	24	4	38	86

REFERENCES

1. Koizumi, H., Iizuka, H., Aoyagi, T. and Miura, Y. (1985) Characterization of adenosine deaminase from normal human epidermis and squamous cell carcinoma of the skin. *J. Invest. Dermatol.* 84, 199-202.
2. Borzenko, B.G. (1991) Use of the study of DNA metabolism enzyme activities as a test system in the treatment of breast cancer. *Sov. Med.* 2, 14-17.
3. Eroglu, A., Canbolat, O., Demirci, S., Kocaoglu, H., Eryavuzm Y. and Akgul, H. (2000). Activities of adenosine deaminase and 5'-NT in cancerous and non-cancerous human colorectal tissues. *Med. Oncol.* 17 (4), 319-324.
4. Bose, C.K. and Mukherjee, M. (1994). Enzymatic tumour markers in ovarian cancer: a multiparametric study. *Cancer Lett.* 77 (1), 39-43.
5. Viot, M., Thyss, A., Ramaiah, A., Cambon, P., Schneider, M., and Lalanne, C.M. (1981) Comparative study of gamma-glutamyl transferase, alkaline phosphatase and its α -L-isozyme as biological indicators of liver metastasis. *Clin. Chim. Acta.* 115, 349-358.
6. Geeta Rathnakumar and Raste, A.S. (2000) Can 5'-Nucleotidase estimation be a predictor of liver metastasis? *Ind.J. Cancer* 37, 23 -27.
7. Giusti, G. (1974) Adenosine deaminase. In: *Methods of Enzymatic Analysis*. Ed: Bergmeyer, H.U. Academic Press Inc., New York 20, 204-229.
8. Raymond, John Wood and David, Gwynne Williams (1981) Colorimetric determination of serum 5'-NT without deproteinization. *Clin. Chem.* 27 (3), 464-465.