GLYCOPROTEIN COMPONENTS IN THE SERUM OF PATIENTS WITH CANCER BREAST

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ABSTRACT

The levels of total sialic acid, lipid bound sialic acid and fucose were estimated in the sera of patients with benign and malignant tumours of breast. An increase was noted in all the three parameters, with a more marked increase in malignancy, when compared with benign and controls. Consequent to surgery, there was an elevation in the serum levels of the above parameters than the values prior to surgery and a decline was noted two months after surgery although none of the values reached the normal range. These results suggest a close association of the glycoproteins with the tumour burden and further signify their role in early detection and staging of cancer breast.

KEY WORDS: Cancer breast, Benign breast disease, Total sialic acid, Lipid bound sialic acid, Fucose, Biomarkers.

INTRODUCTION

Breast tumour in women has shown an increased prevalence world-wide, both in industrialized and developing countries (1). Over the years a large number of risk factors have been identified to be associated with the increased incidence of breast cancer. They include demographic (2), anthropometric (3), dietary factors (4), menstrual and reproductive pattern (5, 6), lack of breast feeding (7), hormonal changes (8) and familial inheritance (9).

Detection of these tumours today, chiefly relies on self examination, physical examination by trained health personnel, mammography and fine needle aspiration cytology all of which having their own limitations. Hence, there is need for alternative, non invasive, sensitive methods to detect growths small in size which escape routine examination. This could be achieved to a certain extent by measuring products of biochemical nature derived from tumours. Blood levels of glycoproteins have been extensively studied for their importance as cancer markers in

breast (10). However, no single biochemical marker has as yet proved to be useful in the diagnosis of neoplastic disease (11). Also review of scientific literature indicates lack of sufficient information on the assessment of glycoprotein related substances as biomarkers for breast cancer.

The aim of the present study was to analyse serum levels of these macro-molecules to assess their usefulness as tools in the early detection and staging of breast tumours.

MATERIALS AND METHODS

The study was conducted on patients with diseases of the breast, admitted to the surgery department of Medical College Hospital, Thiruvananthapuram. The clinical diagnosis was later confirmed by histopathological examination. Malignant tumours were graded as per TNM classification adapted by International Union of Cancer and American Joint Commission in Cancer. The normal, control group consisted of women in the age group of 20-65 years, with no evidence of malignancy, bacterial infections or rheumatoid disease.

10 ml of blood was collected under aseptic conditions by venepuncture and without any antico

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Table 1: Age related classification of normal subjects and breast cancer patients.

Age in years	Number of cases				
	16-25	26-35	36-45	46-55	>55
Normal	4	29	2	2	3
Benign FCD	1	6	10	3	-
FA	5	5	8	1	1
Malignant Stage I	-	2	4	5	4
Stage II	-	1	7	2	5
Stage III	-	1	2	5	4
Stage IV	-	1	4	1	4

FCD = Fibrocystic disease, FA = Fibroadenoma, —Nil

agulant from each of these women, at the time of admission. Subsequently 7 days and 2 months after surgery, blood samples were collected from patients with histopathologically confirmed breast cancer. The serum separated at room temperature was used for analysis within twenty-four hours of collection.

All chemicals used were of reagent grade. Total sialic acid (TSA) was estimated by thiobarbituric acid method of Warren (12), lipid bound sialic acid (LBSA) by resorcinol method (13), and fucose by cysteine-sulphuric acid method (14).

RESULTS

Age related distribution of breast tumours in women presented in Table 1 indicates a clear distinction with regard to benign breast tumours. The inci-

dence of former was higher in the younger age group patients. Cancer of the breast shows as increased incidence with age. This is further supported by the fact that no case of malignancy of breast was observed in women in the younger age group of 16-25 years.

Serum levels of TSA (Table 2) show an increase above normal in all types of breast tumours studied ($p < 0.001$). However this increase was much higher in women with malignancy compared to those with benign tumours ($p < 0.001$). Further, a serial increase in the serum levels of TSA was observed in malignant breast tumours, stage I to IV ($p < 0.001$). Values of serum TSA of malignant tumours remain above normal even 2 months after surgery, the reasons for which are unclear at present due to lack of further follow-up studies.

Table 2: Total serum sialic acid (TSA) levels in breast cancer patients pre and postsurgery.

		No. of cases	Pre-surgery	Post-surgery	
				7 days	2 months
Normal		40	1.5 ± 0.03	-	-
Benign	FCD	20	1.8 ± 0.06	2.6 ± 0.05	-
	FA	20	2.6 ± 0.06	3.2 ± 0.07	-
Malignant	Stage I	15	5.7 ± 0.09	6.4 ± 0.09	2.7 ± 0.18
	Stage II	15	6.6 ± 0.05	7.1 ± 0.05	2.5 ± 0.1
	Stage III	10	7.5 ± 0.12	8.0 ± 0.15	2.4 ± 0.14
	Stage IV	10	9.7 ± 0.19	10.7 ± 0.20	7.6 ± 1.44

a. Values are Mean $\pm$ SeM, expressed as μ mol/L serum.

b. Difference between normal and tumour patients, between patients with benign and malignant tumour and between various stages of malignant breast tumours are statistically significant, $p < 0.001$.

- Not done

Table 3: Lipid bound sialic acid (LBSA) levels in serum of patients with breast cancer pre and post surgery.

		No. of cases	Pre-surgery	Post-surgery	
				7 days	2 months
Normal		40	14.0 ± 0.05	-	-
Benign	FCD	20	14.8 ± 0.07	16.0 ± 0.21	-
	FA	20	16.6 ± 0.16	18.0 ± 0.06	-
Malignant	Stage I	15	20.8 ± 2.28	22.9 ± 1.27	14.9 ± 0.23
	Stage II	15	24.2 ± 0.41	24.1 ± 1.57	17.3 ± 0.68
	Stage III	10	30.8 ± 0.12	32.3 ± 0.83	15.6 ± 0.29
	Stage IV	10	37.9 ± 0.19	40.0 ± 0.53	30.3 ± 3.95

- a. Values are Mean ± SEM, expressed as mg/dl serum.
b. Difference between normal and tumour patients, between patients with benign and malignant tumour and between various stages of malignancy are statistically significant, [$p < 0.001$].
— Not done

Table 4: Serum fucose concentration in patients with breast cancer pre and post surgery.

		No. of cases	Pre-surgery	Post-surgery	
				7 days	2 months
Normal		40	40.7 ± 0.5		-
Benign	FCD	20	57.1 ± 0.6	64.0 ± 0.8	-
	FA	20	66.8 ± 0.5	71.4 ± 0.3	-
Malignant	Stage I	15	48.4 ± 1.13	50.7 ± 1.1	41.4 ± 0.3
	Stage II	15	84.2 ± 1.7	89.7 ± 2.0	70.3 ± 1.57
	Stage III	10	113.5 ± 11.84	116.4 ± 12.15	77.3 ± 3.85
	Stage IV	10	136.9 ± 13.6	136.9 ± 2.1	109.5 ± 11.5

- a. Values are Mean ± SEM, expressed as mg/ml serum.
b. Difference between normal and tumour patients, between patients with benign and malignant tumour and between various stages of malignant breast tumours are statistically significant, [$p < 0.001$].
— Not done

Similar type of changes were observed with regard to serum levels of LBSA (Table 3) and of fucose (Table 4) in women with different types of breast tumours. Seven days after surgery all these parameters were found to be elevated in serum in all types of tumours studied when compared to pre-surgery values. Further, even 2 months after surgery of malignant breast tumours, serum levels of LBSA and fucose did not return to normal values for stage II to IV malignancy. Normal levels were only seen for Stage I tumours which suggests

a possible influence of the tumour stage on the return of these serum parameters to normal with time.

DISCUSSION

The present study clearly indicates that serum levels of TSA, LBSA and fucose in breast tumour patients are significantly elevated above their normal serum levels confirming their usefulness as biomarkers for this disease. The glycoprotein related parameters

are well established as useful markers for diagnosis of various types of cancers (15,16). However, none of these investigators have studied all the three parameters together as a possible tool in the diagnosis or prognosis of breast tumours. The results of the present investigation have suggested the utility of serum levels of TSA, LBSA and fucose as a diagnostic marker for confirmation of suspected breast tumours without the need for tissue invasive techniques.

Further, the extent of difference in serum levels of TSA, LBSA and fucose observed between patients with benign breast tumours and malignancy is significant suggesting their importance for differential diag-

nosis of the type of breast tumours. Lack of regression in the serum levels of these three parameters 7 days after surgery where all cases show an increase in their levels, may be due to cell shedding or acute phase reaction to surgery. Such an observation has also been documented by other investigators with various cancers (17). A significant decrease in the serum levels of these parameters 2 months after surgery of malignant breast tumours is supportive of their conclusion. However, lack of return of most of these parameters to normal serum values even after 2 months surgery remains unexplained at present and requires further follow up of cases.

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