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CA-50 serum level in patients with prostate cancer*

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Summary. CA-50 antigen is considered to be a generalized carcinoma-associated antigen. CA-50 serum levels were measured by solid phase radioimmunoassay using a specific monoclonal antibody. Sera of 49 patients with prostatic cancer of different clinical stages, 43 patients suffering from BPH, and 28 healthy males were tested. Positive test results were observed in 57.1% of patients with prostate cancer values ranging from 42.9% in stage A to 66.7% in stage D. Increased CA-50 levels were found in 11.6% of patients with BPH.

Key words: CA-50 antigen – Biochemical tumor markers – Prostate

In oncology biochemical diagnosis requires the determination of tumor markers in plasma. Prostatic acid phosphatase [PAP] and prostatic specific antigen (PSA) are generally accepted markers for prostate cancer. The prevailing opinion is that determination of carcinoembryonic antigen (CEA) as well as tissue polypeptide antigen (TPA) in prostate cancer are of minor value and may be applied only complementary to PAP or PSA [2, 6, 8–11].

The concept of monoclonal antibodies created new possibilities in the search for tumor-associated antigens [3]. At the turn of 1983 and in 1984 a group of Swedish authors published a series of papers describing the new tumor-associated antigen CA-50. In preliminary investigations they reported a high percentage of increased serum level of CA-50 in prostatic cancer [4]. However, some of the later reports did not confirm this phenomenon [10].

The present report deals with the results obtained in patients with prostate cancer and those suffering from benign prostatic hyperplasia (BPH).

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Materials and methods

Serum for CA-50 determination was performed in patients suffering from prostatic cancer of different clinical stage ($n = 49$), in patients with BPH ($n = 43$), and clinically healthy and biochemically normal males ($n = 28$). In all cases the diagnosis was microscopically confirmed (examination of surgically removed hyperplastic glands, material obtained during TUR or by fine needle biopsy). The patients with cancer were staged according to the modified Whitmore's clinical classification [12]. The age of cancer patients ranged from 58 to 83 with the median of 71 years, in BPH patients from 54 to 84 with the median of 72 years, and in healthy males from 38 to 77 with the median of 68 years.

Blood specimens were obtained by standard procedure, i.e. prior to treatment. Serum samples were stored at −30°C until used.

CA-50 levels were determined by solid phase radioimmunoassay according to the inhibition procedure, with the CanAg RIA kits manufactured by Stena Diagnostics [1]. The radioimmunoassay was based on the ability of serum containing CA-50 antigen to inhibit binding of C50 monoclonal antibody (Mab) to plastic-adsorbed purified CA-50 ganglioside antigen; an antimouse immunoglobulin preparation labeled with radio-iodine was used to detect the bound, uninhibited C50 Mab. Radioactivity was determined in a Beckman Instrument Model 8500 gammascintillation counter. The results were expressed as the percentage inhibition to the C50 Mab. All determinations were done in duplicate. Precision of the test was ±1.8 percentage inhibition.

The results were analysed using statistical methods and criteria. The significance of differences among groups was estimated using the nonparametric Kruskall-Wallis H test. The range of normal at 95% percentile is 0.0–24.8 percentage inhibition. Values over 24.8 percentage inhibition were considered as elevated or as "positive results of the test" [13].

Results

Table 1 shows the median values of CA-50 concentration in patients with prostatic cancer of different stages, those with BPH, and in healthy males. Table 2 summarizes the results of statistical evaluation of results.

It is evident that in the group of prostatic cancer patients (all stages) there is a significant elevation of CA-50 compared with BPH patients as well as compared with the group of healthy males.

Table 1. Results of radioimmunoassay inhibition tests for CA-50 values in serum samples from patients with prostate cancer, BPH and healthy males

Group	Median value (percentage inhibition)	Range of values (percentage inhibition)
Prostate cancer	28.3	1.2–85.6
stage A	22.1	4.7–50.3
stage B	28.5	2.7–74.1
stage C	28.6	1.2–65.8
stage D	28.3	6.3–85.6
BPH	10.9	0.0–35.4
Normal	14.0	0.0–26.4

Table 2. Results of statistical evaluation (Kruskall-Wallis H test)

Comparison groups	Normal	BPH
	(H test values)	
Prostate cancer	17.81***	19.27***
stage A	8.82**	7.82**
stage B	11.32***	11.83***
stage C	8.11**	4.89*
stage D	7.05**	9.33**
BPH	0.06	-

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

Table 3. Summary of positive tests for CA-50 plasma concentration

Group	No tested	No (%) positive
Prostate cancer	49	28 (57.1%)
stage A	7	3 (42.9%)
stage B	21	12 (57.1%)
stage C	12	7 (58.3%)
stage D	9	6 (66.7%)
BPH	43	5 (11.6%)

Table 3 summarizes numbers and percentages of positive results of the test; the clinical stage of cancer is also considered. Positive test results were observed in 57.1% of the patients. But there were some differences among the stages, the lowest percentage being noted in stage A and the highest in stage D. Although there were no significant differences of CA-50 concentrations in patients with BPH compared with healthy males, 11.6% of them showed positive results. The details are presented in Fig. 1. Only the cancer patients, especially in stage D, showed highly elevated values.

Discussion

The hybridoma technique for producing monoclonal antibodies has dramatically improved the possibility of

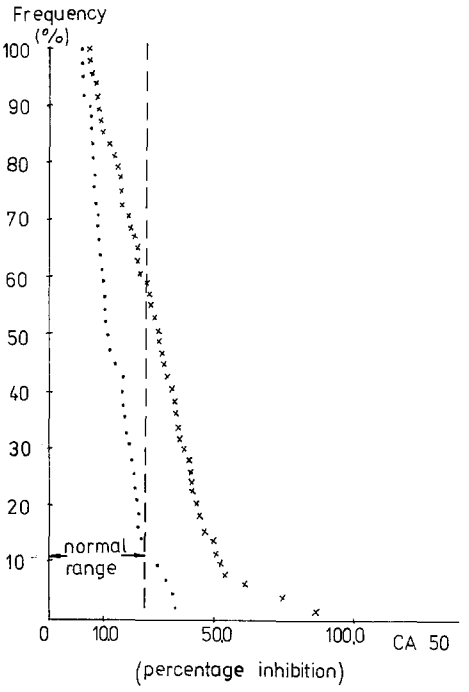

Fig. 1. Inverse distribution of the results of radioimmunoassay inhibition tests for CA-50 values in serum samples from patients with prostate cancer (×) and patients with BPH (·). Dashed line marks the upper limit of normal range

preparing specific immune reagents against tumor-associated antigens [3, 5]. In a program to identify and characterize tumor-associated glycoconjugate antigens by means of monoclonal antibodies Hølmgren et al. detected a monoclonal antibody C50 raised against a colorectal adenocarcinoma cell line that defined the tumor-associated carbohydrate antigen CA-50. It has been demonstrated in carcinomas originating not only from colon but also from pancreas, stomach, lung, prostate, kidney , urinary bladder and mammary glands. The CA-50 has not been found in nonepithelial tumors. Thus, CA-50 appears to be generalized carcinoma-associated antigen which is not restricted to any particular organ.

With the RIA inhibition test it has been shown that the serum concentration of CA-50 in healthy people does not exceed 17 units/ml.

The clinical data concerning CA-50 serum level are rather scarce. There is growing evidence that the determination of serum levels may be of value in the management and prognosis of patients suffering from cancer originating from different sites. Elevated levels of this antigen have been first demonstrated with high frequency in patients with primary or metastatic cancer, but rarely in other diseases. Then highest percentage of significantly increased values of CA-50 was found in pancreatic, colorectal and prostatic cancer – i.e. 70 to 100% of patients. The frequency of elevated values is considerably lower in patients with breast, urinary bladder and kidney carcinoma. In nonmalignant diseases a small percentage of increased values (3–7% of patients) is reported.

Our test series yielded similar results in healthy males as those published by others. The percentage of increased

results in our group of prostate cancer patients has been 57% and ranged, depending on stage, from 42.9% in stage A to 66.7% in stage D. It was lower than the data published by Hølmgren and al., who found raised values of CA-50 in 90% of patients with prostate cancer. These authors found increased concentrations of CA-50 in 75% of patients with stage A, and in all patients with disseminated tumor [4, 7]. Quite different results were published by Stromme et al., who found increased CA-50 serum level in only 20% of prostate cancer patients [10].

In this study we found increased values of CA-50 in 11.6% of patients suffering from BPH. Compared with prostate cancer only moderately increased levels of CA-50 were observed (Fig. 1). Therefore, our results were similar to those published by Stromme et al. [10].

In conclusion, our results are neither as optimistic as presented by Hølmgren et al. [4], nor as pessimistic as reported by Stromme et al. [10]. However, it appears that CA-50 determination in serum of patients with suspected prostatic cancer is not superior to TPA and CEA test.

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