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Assessment of tumor markers in patients with chronic renal failure

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ABSTRACT

In this study; serum levels of different tumor markers such as alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA), cancer antigen 125 (CA 125), cancer antigen 19-9 (CA 19-9), cancer antigen 15-3 (CA 15-3), and prostate-specific antigen (PSA) in 36 predialysis, 42 hemodialysis (HD), 42 continuous ambulatory peritoneal dialysis (CAPD) patients and 32 healthy volunteers as control group who did not present any clinical symptoms or signs of neoplasia with negative hepatitis markers were studied. The mean serum levels of CEA and CA 19-9 were found to be higher than the control group in predialysis, HD and CAPD patients. Serum levels of CA 125 in CAPD group was found to be higher as compared to the other groups. Serum AFP, CA 15-3 and PSA levels were similar in all groups. In conclusion, serum tumor markers do not have any diagnostic utility and may be unreliable for monitoring malignancies in uremic patients. [Turk J Cancer 2007;37(4):143-147]

KEY WORDS: Chronic renal failure, predialysis, hemodialysis, continuous ambulatory peritoneal dialysis, tumor marker

INTRODUCTION

A variety of renal diseases and electrolyte disorders may be associated with various malignancies or with treatment of malignancy by chemotherapeutic drugs or radiation. In literature, comparison studies with control groups of having no chronic renal failure (CRF) showed that risk of the cancers of kidney, corpus uteri, prostate and multiple myeloma were increased in patients with CRF. Moreover, increased risk of transitional cell tumors of renal pelvis in analgesic nephropathy patients, of non-Hodgkin's lymphomas (NHL) in glomerulonephritis patients and of brain tumors, Kaposi's sarcoma and NHL in transplant patients were reported in some studies (1-4).

The concentration of tumor markers in human sera is affected not only by malignant, but also by many benign diseases. In this regard, only few reports exist about renal insufficiency, whereas influences of different benign diseases have frequently been described. Serum levels of some tumor markers could be abnormal without malignancy because of disturbed metabolism. Hence, some tumor markers may not be valuable in both the diagnosis and follow-up due to their abnormally high levels while some may be beneficial in diagnosis due to their normal serum levels, and also serum levels of some tumor markers may be high before dialysis while they may decrease after dialysis (2, 5-8).

In the present study, we aimed to compare the levels of alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA), cancer antigen 125 (CA 125), cancer antigen 19-

9 (CA 19-9), cancer antigen 15-3 (CA 15-3), and prostate-specific antigen (PSA) in predialysis, hemodialysis (HD), continuous ambulatory peritoneal dialysis (CAPD) patients and healthy volunteers.

MATERIALS AND METHODS

Thirty-six predialysis (19 female, 17 male), 42 HD (23 female, 19 male), 42 CAPD (24 female, 18 male) patients, in regular follow-up program for CRF, who were nonsmokers, with no clinical or biochemical evidence of neoplasia with negative hepatitis markers, and a control group composed of 32 healthy volunteers (17 female, 15 male) who were also nonsmokers, with no clinical or biochemical evidence of neoplasia with negative hepatitis markers were enrolled. Fasting blood samples were drawn from the patients and the control group to detect serum levels of AFP, CEA, CA 125, CA 19-9, CA15-3 and PSA at 8:00 a.m.

Patients in HD group were in three times per week, four hours duration bicarbonated hemodialysis program using hemophan dialysers with capillaries of 1.2 m^2 surface area (Hollow-Fiber). CAPD patients were administered three or four times in a day 2-2.5 liters of peritoneal dialysate solutions composed of 1.36% and in case, 3.86% glucose. Patients were on 30-35 kcal/kg/day CRF diet composed of protein 0.6 g/kg/day for PD, 1.2 g/kg/day for HD, and 1.4 g/kg/day for CAPD, and 1000-1500 mg/day calcium, 600-700 mg/day phosphorus, 200-250 mg/day magnesium.

Tumor markers were studied in "Technicom RA-XT" autoanalyser by using specific "chemiluminescent" enzyme immunoassay kits (Immulite) for each tumor marker. Normal laboratory values were; 0.2-7.0 U/ml for AFP, 0.0-3.4 ng/ml for CEA, 1.7-32 U/ml for CA 125, 2.5-33 U/ml for CA 19-9, 7.5-53 U/ml for CA 15-3, and 0.4-4 ng/ml for PSA.

The results were analyzed by using a software program "SPSS for Windows Version 9.0". Data were represented as mean±SD. Student's-t test was utilized for the comparison between the groups.

RESULTS

The distribution of mean ages, gender, follow-up periods and CRF etiologies of 36 predialysis, 42 HD, 42 CAPD and 32 healthy volunteers as control group were demonstrated in table 1. In terms of age distribution and gender diversity, groups were similar.

Mean serum levels of AFP, CEA, CA 125, CA 19-9, CA 15-3, and PSA in predialysis, HD, CAPD and control groups were shown in table 2. While there was no

Table 1
Basic clinical characteristics of the study population

	Predialysis (n=36)	HD (n=42)	CAPD (n=42)	Control Group (n=32)
Age (year)	36.8±12.8	42.7±13.9	43.6±13.6	42.5±12.4
Gender (Female/Male)	19/17	23/19	24/18	17/15
Median follow-up time (months)	16.3±11.0	18.5±16.0	21.8±14.0	-
Primary disease				
Primary glomerulonephritis	9	7	8	-
Diabetic nephropathy	11	13	12	-
Hypertensive nephropathy	6	3	5	-
Polycystic kidney disease	5	6	6	-
Amyloidosis	3	1	1	-
Reflux nephropathy	2	2	2	-
Unknown	-	10	8	-

Table 2
Mean serum levels of tumor markers in study groups

	Predialysis	HD	CAPD	Control Group
AFP (ng/ml)	0.8±0.5	1.1±0.9	1.1±0.5	0.8±0.3
CEA (U/ml)	1.6±0.2	3.0±0.4	2.7±0.4	0.7±0.3
CA 125 (U/ml)	10.6±6.1	12.8±9.7	22.8±6.6	8.3±4.5
CA 19-9 (U/ml)	14.4±11.3	18.6±10.1	17.8±12.1	7.0±9.6
CA 15-3 (U/ml)	29.8±12.8	31.6±13.5	28.5±12.5	25.0±12.5
PSA (ng/ml)	1.9±0.9	2.1±1.1	2.2±1.0	1.8±1.1

difference in serum levels of CEA and CA 19-9 between predialysis, HD and CAPD groups ($p>0.05$), they were higher in patient groups as compared to the control group ($p<0.05$). Mean serum levels of CA 125 was higher in CAPD patients than the other groups ($p<0.05$). There was no difference in serum AFP, CA 15-3 and PSA levels between the groups ($p>0.05$). In addition, serum tumor marker levels were within normal limits in all groups.

DISCUSSION

Tumor markers are hormones, enzymes, metabolites, immunoglobulins, various proteins, tumor associated antigens, oncogenes and substances that are helpful in the detection and diagnosis of certain cancers. Despite the plethora of proposed tumor markers, only a few have achieved clinical relevance (9).

AFP in fetuses is biochemically related to albumin in adults. It is found in fetal liver, yolk sac, and the gastrointestinal tract. Consequently, AFP is correspondingly increased in about 80% of patients with hepatomas, 60% of patients with nonseminomatous germ cell cancers, and occasionally in patients with other cancers. In many studies, the serum levels of AFP have been shown to be unaltered in patients with CRF and our results are consistent with literature data (6,10-12).

CEA, a fetal glycoprotein found on cell surfaces, is produced in the fetal gastrointestinal tract, pancreas, and liver. It is present in small quantities in the blood and in cells of many normal adult tissues. It is a useful marker for monitoring breast, colon, and lung cancers. Elevations of CEA blood levels are found in smokers and in patients with chronic obstructive lung disease, inflammatory or peptic bowel disease, liver inflammation or cirrhosis of any cause, and fibrocystic breast disease. While some studies have concluded that CEA levels are elevated above normal values in patients with CRF by 5-90% due to deteriorations in elimination, in the study by Arık et al. (5) these levels were normal (2,6,10-11). In the present study, the mean serum level of CEA was found to be higher than the control group in predialysis, HD and CAPD patients. We think that higher levels of serum CEA levels in patients group compared to that of the control group is due to insufficient elimination of CEA through the kidneys, dialysis membranes and peritoneum.

CA 125 is useful for monitoring patients with known ovarian cancer when blood levels correlate closely with extent of disease, response to therapy, and recurrence. It is useless as a general screening test for ovarian cancer. Less than 1% of healthy women have blood levels of more than 35 U/mL. Furthermore, women with a variety of other epithelial cancers have a significant prevalence of elevated CA 125 serum levels. Elevated levels are also found in lymphomas, liver diseases, a variety of inflammatory conditions, benign tumors, and pregnancy (13). CA 125, which points out to the proliferation of mesothelial cells, is reported to be an appropriate tumor marker in CAPD patients (14). It is also reported to increase in patients with CRF due to fluid overload (15). In the present study, the mean serum CA 125 levels were elevated in CAPD patients when compared to the control and other groups. The average duration of dialysis in CAPD patients were found to be 21.8±14.0 months and 16 patients were found

to have experienced an attack of peritonitis once, 4 patients twice and 2 patients, three times. However, despite the high value of mean ratios, all patients had CA 125 levels within normal limits (Table 2). Earlier studies show that the risk of peritonitis increases both in adult and in pediatric CAPD patients and the number of mesothelial cells decreases as the duration of peritoneal dialysis increases. Also no correlation was shown to exist between the levels of CA 125 and the number of peritonitis attacks. Because of this, it is reported that CA 125 levels may be elevated at the beginning of CAPD and may eventually decrease as the duration of dialysis increases (16,17).

CA 19-9 is a Lewis blood group antigen that is found in increased levels in gastrointestinal cancers. It is first detected in patients with colorectal cancer, while it is reported to be elevated in pancreatic and gastric cancers as well. It is helpful in the diagnosis and monitoring of pancreatic cancer, in which it has a 70% specificity and a 90% sensitivity. In literature, it is mostly seen that it maintains its clinical value in CRF, except in two studies (5,6, 10-12,18) where its levels were found to be elevated. In the present study, while no significant difference was detected in the mean serum CA 19-9 of patients in the predialysis, hemodialysis and CAPD groups, the values were significantly higher in patients groups compared to that in the control group. However, serum values of CA 19-9 were within normal limits in all of the patients.

CA 15-3 is structurally a glycoprotein that is principally detected by immunoabsorption and may be elevated in patients with breast, ovarian, prostate, and lung cancer and is also reported to be increased in hepatitis conditions (2,11,15). Arican et al. (19) reported that CA 15-3 levels were elevated in 6% of patients, of which 27 were anti-HCV positive and 23 were negative. In the present study, no significant differences were detected in serum CA 15-3 levels among the study groups. The reason why the tumor markers were within normal limits in the present study may be that our patient series were composed of patients with negative hepatitis serology. In many studies, the serum levels of CA 15-3 have been shown to be unaltered in patients with CRF and our results are consistent with literature data.

PSA is a serine protease, which is produced by prostatic alveolar and ductal epithelial cells and correlates closely with tumor bulk and response to therapy for men with prostate cancer. Its serum levels are reported to be stable in most patients with CRF and therefore it may be useful in the diagnosis (5,6,8,10,11). In our study, although PSA levels were found to be higher than that in the control group, levels in all patients were within normal limits which were consistent with literature.

In a study conducted among hemodialysis patients with acquired renal cystic disease, Polenacovic et al. (20) reported that tumor markers do not exhibit a significant difference between a group with cystic disease and other groups. In our study simple renal cysts were not evaluated, as tumor markers were within normal limits in all patients and patients with polycystic renal disease were included in the study groups as well.

In conclusion, serum levels of CEA and CA 19-9 were found to be higher in patients with CRF as compared to the control group. Also, levels of CA 125 were higher in CAPD patients than in the control and other groups. It is concluded that the serum levels of tumor markers do not have a diagnostic value in patients with CRF. We consider that serum levels of tumor markers should not be measured in patients without a suspicion of malignancy, except for research purposes.

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