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Prognostic Importance of Prostate-Specific Antigen in Cancer Prostate Patients

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Abstract

Serum PSA was measured by radio immuno assay in 52 patients with cancer prostate, 22 patients with regionally confined disease and 30 patients with (stage D2) advanced lesion. The results indicated that there was no significant difference between normal range of serum PSA and the group of patients, remained disease free during follow-up period. On the contrary, patients relapsed after initial treatment showed highly significant elevation of PSA in relation to the normal range ($p > 0.001$). There was also significant risk between elevated PSA level and disease progression in advanced diseases (stage D2) patients. The results indicate that PSA is a valuable marker in patients with prostate cancer not only diagnostic but also as prognostic indicator.

Introduction

IT is indeed unfortunate that most prostate cancer patients are diagnosed with disseminated disease [1].

Although the search for a reliable tumor-specific marker of malignancy in prostate cancer patients has continued for over 30 years, studies of serum markers have not substantially improved the survival rate of these patients [2].

However, several recent studies [3,4], have statistically verified an improvement in the prognostic value of tumor markers in patients with prostate cancer.

If a tumor marker, among other criteria, is to be useful for diagnosis of patients with prostate cancer, it should be specific for malignancy, indicative of prognosis and reflective of the patients tumor-bearing status [5].

Prostate-Specific Antigen (PSA) was recently introduced for monitoring of disease and for differential diagnosis of metastasis in prostate cancer patients [6]. Several studies have shown PSA to be useful also for monitoring of treatment response in these cases [2,7].

PAS was first identified by Wang and his co-workers [8] at Rosewell park memorial institute in 1979. Although similar quantities (approximately 11.0 mg/gm of

tissue) of PSA are found in normal, benign and malignant prostate tissue [7], the antigen is restricted in the prostate to the cytoplasm of the ductal epithelium and to secretions in the ductal lumina. Since PSA is prostate-specific and a secretory portion, it may be recovered and purified from both prostatic tissue and seminal plasm [9]. Antibody directed against purified PSA binds to normal, malignant, or metastatic prostatic tissue but does not bind to other normal or malignant tissues [6,9]. The biochemical identity of PSA has been established [10] and its basic characteristics have been described [8,9]. Unlike prostatic acid phosphatase (PAP), PSA has not been demonstrated in other tissues and malignancies [2].

The aim of this work is to study the prognostic value of prostate-specific antigen (PDA) for monitoring of treatment response in prostate cancer patients.

Patients and Methods

The study was carried out on 52 consecutive prostate cancer patients who were referred to Kasr El-Eini Center of Radiation Oncology and Nuclear Medicine (NEMROCK), Cairo University during the period from 1 st of Jan. 1990 to the end of Dec. 1990. All patients were subjected to clinical examination, laboratory studies, radiological examinations, radio-nuclide bone scanning and histopathological confirmation for diagnosis.

Serial estimation of serum PSA was carried out in all patients before start of definitive treatment, shortly after termination of primary treatment and periodically during follow-up period. PSA was determined by RIA technique [11].

Evaluation of response and relapse was determined both by clinical examination and various laboratory or imaging investigations according to the judgment of the treating physician.

Regionally confined tumors were initially treated by transurethral resection (TUR) or open prostatectomy according to the disease extent and decision of the treating urologist.

This was followed by post-operative radiotherapy using either telecobalt gamma rays or 10 MV photons. The treatment volume was including the whole prostate and all regionally involved tissues using beam directed multiple portals. The mean tissue dose to pelvis ranged between 50-55 Gy over 5-6 weeks in 25-30 fractions, 5 fractions per week. The prostate and immediate surrounding tissues received a dose of 65-70 Gy over 6, 5-7, 5 weeks.

Advanced stage disease cases (stage D2) were treated by various hormone measures with or without external irradiation to painful bony metastasis according to the treating physician policy.

The relation between serum PSA and clinical state of patients in the follow up period was studied.

Results

The main clinical characteristics of the whole study group is shown in table 1.

Regionally confined prostate cancer group (22 patients):

A total of 116 serum samples were analyzed for PSA levels for these patients over a two years period of follow up. The mean follow up time for this group was 7.6 months with a range of 3-24 months.

Twelve patients (55%), remained disease-free while 10 (45%) relapsed either

locally (4 patients) or at distant sites (6 patients), Table 2.

The mean value of serum PSA for the disease free cases during the follow-up period was 7.47 ± 5.9 ng/ml. While it was 102.96 ± 43.3 mg/ml for relapsing cases. The difference was statistically highly significant (p <0.0001).

The relation between pre, post treatment and follow-up serum PSA levels to treatment response is shown in table 4.

Metastatic disease: (30 cases):

The serial PSA measurements in advanced group patients showed also a highly significant relationship between elevated PSA levels and risk of disease progression (p <0.001), (Table 5). Examples of typical changes occurring during treatment, are illustrated in (Fig. 1), which showed PSA elevation shortly before discovery of positive bone scan.

Table (1): Clinical Characteristics of 52 Cancer Prostate Patients.

	Regionally confined	Matastatic disease
Total No.	22	30
Mean age	52.9 ± 6.6	56.8 ± 7.4
Well differentiated	9	7
Moderately differentiated	5	9
Poorly differentiated	8	14
Confined to prostate	6	-
Spreading to immediate adjacent tissue	8	14
Spreading to other pelvic organs	8	16
Bone metastasis	0	18
Liver metastasis	0	7
Lung metastasis	0	5

Table (2): Overall Treatment Results in Patients with Regionally Confined Prostate Cancer patients (22).

Total No. of patients	No evidence of disease		Treatment failure					
			Over all		Loco-Regional		Distant	
	No.	%	No.	%	No.	%	No.	%
22	12	55	10	45	4	40	6	60

Mean observation time 7.6 months ± 4
Range of follow up 3-24 months

Table (3): Regionally Confined Cancer Prostate Cases Mean Serum PSA Level in D.F. and Failing Patients.

	Disease free cases (12 patients)	Failing cases (10 patients)
Mean level of PSA (ng/ml)	7.47 ± 5.9	102.96 ± 43.5

$p > 0.0001$

Table (4): Relation between Serum PSA and Results of Treatment.

Disease free cases (12 patients)			Local recurrence (4 patients)			Distant metastasis (6 patients)		
Before treatment	After treatment	During F.U.	Before treatment	After treatment	During F.U.	Before treatment	After treatment	During F.U.
124± 17.5	5.72± 1.7	7.47± 5.9	164± 36.3	6.6±3 .9	77.4± 39.6	139.9 ±247	6.1±3 .4	128.3 ±30.2

$p > 0.001$

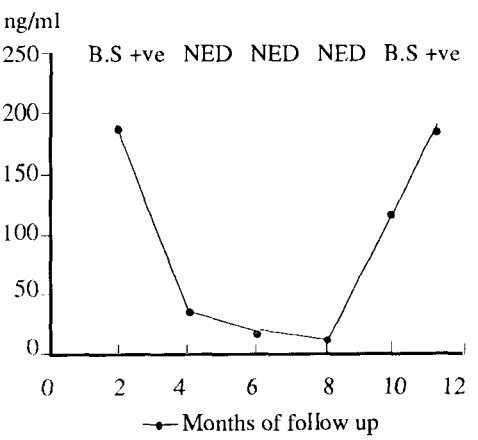

Fig. (1): Exapmle of serial PSA serum levels at the time of treatment of advanced disease.
B.S = Bone scan.
NED = No evidence of disease.

Table (5): Metastatic Disease (30 Patients) Mean Serum PSA Level in Controlled and Progressive Disease Patients (During Follow-Up Period).

	Controlled cases (6 cases)	Progressive cases (24 cases)
Mean level of PSA (ng/ml)	9.8 ± 3.5	104.4 ± 45.6

$p > 0.001$

Discussion

Biological markers have traditionally been used in the follow-up of patients with prostate cancer. Because of the limitations of serum PAP, variations in the measurement of this marker have not been accepted as the sole objective criterion of response in prostate cancer [11]. PSA is a valuable marker in patients with prostate cancer, where Wang et al. in 1979, proved that PSA is the most useful marker in prostate cancer [8].

The results of the present study point to the importance of PSA as a specific marker, especially in monitoring of prostate cancer patients during follow-up. A similar evaluation by Killian and associates [2], in patients with localized or regional disease (ranging from stages B2 through D1), revealed that serial measurement of PSA after definitive therapy was the most significant predictor of the disease-free interval. This observation provides valuable information on the use of this marker to suspect recurrent disease [4].

The present study also revealed a significant relationship between elevated PSA level and risk of disease progression in advanced disease (stage D2 disease) patients. In agreement with this finding is the report of Killian et al. [2] who mentioned that, there was significant association between the risk of progression or death and any PSA level elevated to at least the normal mean + 5 SD (standardized value "SV"), 5 patients with such a PSA level having a risk of disease progression 4.9 times greater than that of advanced-stage patients without elevated PSA levels.

Positive predictive value and time to recurrence are other useful parameters to evaluate the effectiveness of serial measurements of PSA for detection of tumor growth. The data for this parameter were not available and were not analyzed in this study. However, Kuriyama and associates proved a prognostic association between a patient's tumor load and level of PSA [7]. The same authors found a significant relation between the time to recurrence, which was defined as the time between the most elevated level of PSA, measured serially and confirmed recurrence of disease.

Conclusion:

Patients with early-stage cancer of the prostate can be reliably monitored by measuring levels of PSA, not only for detection of progression of the disease but also when PSA levels are normal, for prediction of a favorable prognosis for the next six months. Similarly, a good prognosis may be indicated in advanced-stage patients when PSA level is normal. Conversely, an unfavorable prognosis should be anticipated in advanced-stage patients with elevated levels of PSA.

References

1- GITTES, R.F. and CHU, T.M.: Detection and diagnosis of prostatic cancer. Semin. Oncol., 2: 123-130, 1976.

2- KILLIAN, C.S.; EMRICH, L.J. and VARGAS, F.P.: Prognostic importance of prostate-specific antigen and other markers for monitoring of prostate cancer patients. Cancer Res., 45: 886, 1985.

3- KILLIAN, C.S.; EMRICH, L.J. and YANG, N.: Prognostic importance of prostate-specific antigen for monitoring patients with stages B2 to D., prostate cancer. Cancer Res., 45: 886-891, 1985.

4- KILLIAN, C.S.; EMARICH, L.J. and VARGAS, F.P.: Relative reliability of five serially measured markers for prognosis of pro-

gression in prostate cancer. J. Natl. cancer Inst., 67: 179-185, 1986.

5- JAVADPOUR, N.: Tumor markers in urologic cancer. Urology, 16: 127-136, 1980.

6- NADJI, M.; TABEI, S.Z. and CASTRO, A.: Prostate-specific antigen: An immunohistologic marker for prostate neoplasms. Cancer, 48: 1229-1232, 1981.

7- KURIYAMA, M.; WANG, M.C. and PAPSIDERO, L.D.: Quantitation of prostate-specific antigen in serum by sensitive enzyme immunoassay. Cancer Res., 40: 4658-4662, 1980.

8- WANG, M.C.; VALENZUELA, L.A.; MURPHY, G.P. and CHU, T.M.: Purification of a human prostate-specific antihgen. Invest. Urol., 17: 159:163, 1979.

9- WANG, M.C.; KURIYAMA, M. and PAPSIDERO, L.D.: Prostate antigen of human cancer patients. Methods cancer Res., 19: 179-197, 1982.

10- WANG, M.C.; LOOR, R.M.; LI, S.L. and CHU, T.M.: Physicochemical characterization of prostate antigen purified from human prostate gland and seminal plasma. IRCS Med. Sci., 11: 327-328, 1983.

11- PONTES, J.E.: Biological markers in prostate cancer. J. Urol., 1037-1047, 1983.