Prostate Specific Antigen And Bone Scan Correlation In The Staging Of Patients With "Carcinoma Prostate".

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The ability of serum prostate specific antigen (PSA) to predict bony metastasis at initial presentation was determined in 25 patients. Eight (32%) patients had bony metastasis at presentation and serum PSA values in all these patients were more than 30 ng/ml. Among these 2 (8%) patients had >100ng/ml serum PSA values. Bone scans are necessary in initial staging but following the diagnosis and treatment this can be replaced by serum PSA level estimation in monitoring the patients with carcinoma prostate.

Key Words :- PSA (Prostate specific antigen) DRE (Digital rectal examination,) PAP, (Prostate acid Phosphatase) TUR (Transurethral Resection) TRUS (Transrectal Ultrasound).

Carcinoma of the Prostate is the second most common malignant tumour in men over the age of 55 years, with autopsy series demonstrating tumour foci in 30% of men by the age 70-years. Uptill now the most sensitive method for detection of localised prostate cancer was Digital rectal examination (DRE) of prostate gland. The disadvantage is that the rectal examination is subjective and may vary with the examiners ability for detection of small tumours[1]. This is especially important in men who would now be candidates for curative therapy with minimal functional loss. An additional problem is that physical examination is not uniformly helpful in staging this disease. In 12-16% of patients with seemingly localised tumours, involvement of seminal vesicles and periprostatic tissue were found at the time of Radical prostatectomy[2].

Presently only 60% of newly diagnosed prostate cancers are Clinically localised and curable by currently available treatments. Thus to reduce the mortality rate of prostate cancer it will be necessary to detect the prostate cancers when they are still organ confined and initiate definite treatment at that time. To achieve this goal the detection of specific tumour markers was required. For more than half a century prostate acid phosphatase (PAP) has been used by urologists as a standard to diagnose and staging of prostate cancer. Acid phosphatse may be produced by red cells, liver, spleen, pancreas, bone marrow and prostate itself. Value of acid phosphatase as a marker for prostate cancer is Limited because it is produced by the normal, hyperplastic and malignant tissue in response to infection, and trauma. Prostate acid phophatase would then fall well below the standard requirements for the tumour markers.(12).

PSA is a glycoprotein with molecular weight between 33000-34000 daltans which was first isolated by Wang et, al, in 1979. They mentioned that it was present in normal, BPH, an malignant prostates. It was not identified in any other human tissue. It is prostate specific and distinct from Prostate acid phosphatase (PAP), so termed prostate specific antigen (PSA). PSA is a glycoprotein containing 93% amino acids and 7% carbohydrates it is made up of 240 amino acids (Osterlings 1991)(8). PSA is a serine protein whose function is probably liquefaction of seminal clots after ejaculation. It has half life of 2.2.-3 days serum PSA is measured by radio-immunoassay and the following assays are now available for determination of serum PSA concentration in blood.

-Prochck PSA
-Tendom - E.PSA
-Irma PSA assay
_Solid phase enzyme linked immunosorbent assay(ELISA))
-Eurogenetics PSA quantitative (ELISA)

As the half life of PSA is 3-5 days so 2-3 weeks may be required for serum PSA concentration to achieve a base line level. DRE has no clinically significant effect on serum PSA levels either immediately or 90 minutes after the examination. Similarly transrectal ultrasound (TRUS) had minimal effect on serum PSA values. However cystoscopic examination has been observed to cause a 4-fold increase in serum PSA values, and needle core biopsy of prostate produce 57-fold increase of PSA levels & prostatitis also raises serum PSA levels. TUR-prostate for BPH causes 33 fold rise in immediate post operative PSA levels. However the long term effect of PSA decreases after operation . As the half life of PSA is long one should wait for atleast 2- weeks for ideal serum PSA level estimation after operation. BPH increases the PSA levels 0.3 ng/ml of BPH tissue, while its levels are raised 10 tires that is 3.5 line cases of carcinoma prostate. (Stamey et, al 1987)[3]

Cooner et al, (1990) have recommended prostate biopsies in all patients having serum PSA values more than 10ng/ml. Levels of serum PSA are proportional to the value of cancer prostate. Scrum PSA levels also increase with advancing pathological state of disease. When it is confined to prostate capsule value is upto 20 ng/ml. In local and distant metastasis of prostatic cancer its value rises from 75-100 or more than 100ng/ml. (Ostarling et al 1991)(8) PSA values estimation has a great clinical usefulness in monitoring the patients after a definite therapy much information have been obtained with PSA in patients after the following.

1. Antiandrogen therapy
2. Radiation therapy

3. Radical Prostatectomy.

Materials And Methods:-

This study was conducted at Urology Department Mayo Hospital Lahore during last year. Twenty Five (25) newly diagnosed patients of carcinoma prostate were included in this study. All the patients were evaluated by complete history and physical examination. The symptoms of prostatic enlargement were evaluated by Modified Bowersky's Prostate symptom score (1977). Digital rectal examination (DRE) of prostate was performed in all these patients with empty bladder in knee elbow position. Upto 25gm prostate was considered small, 26 - 40 grams moderate and more than 40 grams prostate as large size. The hard consistency of gland or hard nodules and fixation of mucous membrane were considered as highly suspicious of malignancy. All the patients were clinically staged prior to any treatment. Staging included whole body bone scan, and the images were interpreted and reported by an experienced radiologist.

Serum PSA levels were estimated in all these patients at the time of diagnosis with histologically proven carcinoma prostate. Three ml of venous blood was taken in a disposable syringe from all these patients. Serum was extracted with a centrifuge and kept at a temperature of 2 8^0c. Serun PSA levels were measured by an immunoenzymetric kit Eurogenetics (ELISA) in a batch system. PSA levels from 10 - 20 ng/ml. were taken as suspicious of malignancy. Its normal value is 0 - 5ng/ml. Any patient having PSA level more then 20 ng/ml was declared as highly suspicious and further investigations were performed in all these cases. The Eurogenetics PSA quantitative is an enzyme linked immunosorbant assay (ELISA) for quantitative measurement of PSA in human serum. This diagnostic kit was used for estimation of serum PSA levels in all these cases.

These patients were treated variously by sub capsular orchidectomy, Anti androgen therapy or TUR-Prostate alone.

Serum PSA values were compared with the bone scan results by (Tc.99m MDP Scanner) assessed with respect to positive or negative predictive values. For determining bony metastasis whole body scintigraphy was performed using Tc 99m labelled methylene diphosphate.

Results

Twenty Five proved cases of carcinoma prostate were admitted in Urology Deptt. Mayo Hospital Lahore with bladder outlet obstructive symptoms or metastatic. complaints. Serum prostate Specific antigen (PSA) level estimation and bone scans were performed in all these patients for evaluation. The age ranged from 55 to 98 years with a mean value of 70 ± 10.63 years. Seven (7) patients (28%) were between 55 to 64 years, Ten (40%)between 65 to 74 years and Eight (8) (32%) cases were from 75 to 98 years of age. (Table - 1)

Table - 1 Age Distribution In Carcinome Prostate

AGE (years)	Patients (n = 25)	Percentage (%)
55 - 64	7	28
65 - 74	10	40
75 - 98	8	32

Mean= 70 years.SD= 10.63 years

Table 2: Prostate Specific Antigen (PSA) In Carcinoma Prostate.

PSA (ng/ml)	Patients (n = 25)	Percentage (%)
4 - 10	2	8
10.1 - 20	1	4
20.1 - 80	14	56
80.1 - 100	6	24
100.1 - 320	2	8

Mean. 61.80 ng/ml. D ± 29.95 ng/ml

TABLE - 3 Relation Of Age With Serum PSA Levels In Carcinoma Prostate

Age (years)	Patients (n = 25)	PSA ng\ml (Mean ± SD)	Percentage (%)
55 - 64	7	69.43 ± 27.27	28
65 - 74	10	53.97 ± 32.05	40
75 and above	8	64.91 ± 32.98	32

There were Seven (28%) patients in the age group of 55 to 64 years and mean PSA level was 69.74 ± 27.27 ng/ml. Ten (40%) patients in the age range of 64 to 70 years had mean PSA value of 53.97 ± 32.05 ng/ml where as 8 patients (32%) were of 75 years and above all mean PSA value was 64.91 ± 32.98 ng/ml. The mean difference between the age groups was found insignificant among all age groups, the relationship was also estimated (r = 0.15) and regression equation was

$$Y(PSA) = 92.30 - 0.43 \times (Age)$$

which was very low and statistically insignificant (P > 0.05).

Bone scan was done in all these patients. Bony metastasis of carcinoma prostate was present in pelvis, vertebrae and ribs in Eight (32%) patients. Among these 8 patients 3 (37.5%) had PSA values between 30 - 47 ng/ml, and the remaining had >80 ns/ul PSA values. The histological findings of transuretherally resected prostate tissue in patients of this study are shown in (Table 4)

Table - 4 Histopathological Findings Of Resected Prostatic Tissue In Carcinoma Prostate

Prostate Biopsy	Patients (n = 25)	Percentage (%)
Adenocarcinoma present absent	25	100
Well-Differentiated	9	36
Moderately differentiated	3	12
Poorly Differentiated	13	52

Nine patients (36%) had well differentiated Adeno carcinoma prostate. It was moderately differentiated in

3(12%) and 13 (52%) of them had poorly differentiated adenocarcinoma prostate. The serum prostate specific antigen levels were positive > then 10 ng/ml in 23 (92%) patients so Serum PSA had 92% True positive rate (Sensitivity) and 8% False negative rate.

Discussion

Serum PSA has been used in the early detection, management and follow up of patients with carcinoma prostate. in an attempt to stage the disease particularly in the patients prior to Radical prostatectomy. (Stamey et al 1989)[3,4]. PSA has been shown to be much more sensitive tumour marker than prostate acid phosphatase for carcinoma prostate with a correlation of stage of disease and proportions of these patients with high serum levels [2]. How ever several studies have shown that there is Considerable overlap between various pathological stages such that PSA alone is unreliable for accurate staging. Data of our study confirm these observations and also that if PSA was used alone for staging, a number of patients with bony metastasis would be missed. A study of Sharer[6]. 1991, quotes that negative accuracy for PSA level of 20 ng/ml to be 92% with the conclusion that PSA levels at 20 ng/ml or less do not require bone scan. In our study all the patients with bony metastasis of carcinoma prostate had serum PSA values more than 30 ng/ml which is compare able with Sharers results of 20 ng/ml of PSA levels in bone metastatic patients although bone biopsies were not performed in these patients to confirm the diagnosis. Similar reports by Siddal et, al (1986)[6] showed that PSA alone is inadequate for staging, particularly in poorly differentiated adenocarcinoma prostate, which does not express PSA. Bone scan must then fox still be advocated as part of the initial staging procedure. The ability of PSA to predict progression of disease had been demonstrated by Evcole et al, (1987)[7], they showed that the Median interval between the elevation of PSA and evidence of disease progression was 6-months. Although repeated bone scans have been advocated in the assessment of treatment response in carcinoma prostate by Fitzpytrick et al, (1978)[8]. Our study results suggests that with the use of PSA this is unnecessary. With a relatively low cut off level of 30 ng/ml for PSA, this will give the negative predictive value of 100% for detecting bony lesion. This value may be high for routine use, and further studies are needed to clarify the most useful cut off value. There can be no doubt that PSA is an excellent marker for disease progression in carcinoma prostate, and that it can be used to monitor the disease activity. following initial staging, whether followed by primary treatment or a curative approach. Our evidence along with other data suggests that PSA may replace the need for bone scan and other prognostic monitors. This will be advantageous for elderly patients, who will ovide a lengthy isotope scan procedure

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