Study of Transrectal Ultrasound Guided Biopsies of Prostate in Correlation with Serum Prostate Specific Antigen Level

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Abstract

Introduction: Carcinoma of prostate is on the rise in India. Serum PSA testing and prostatic biopsy are performed routinely whenever carcinoma of prostate is suspected.

Aims and Objectives: To study the histopathology of prostate biopsies and to correlate the serum PSA levels with TRUS guided biopsy findings of carcinoma and BPH.

Materials and Methods: This was a retrospective study carried out in the department of Pathology at Kamineni Academy of Medical Sciences and Research Centre, Hyderabad, over a period of three years. A total of 128 patients underwent TRUS guided prostate biopsy out of which only 61 cases were considered for the study as they had also undergone simultaneous prebiopsy serum PSA testing. The biopsy findings of carcinoma and BPH were correlated with serum PSA level.

Observations and Results: The mean age for carcinoma and BPH was 66.5 and 64.6 years respectively. A total of 17 (27.8%) cases had serum PSA in the grey zone of 4-10 ng/ml. Among BPH cases, 33.3% showed an elevated serum PSA in the 20.1- 100 ng /ml range. A Gleason score of 3+4 was the most common score and was seen in 63.3% cases. The mean PSA for carcinoma was 48.7 ng/ml. High serum PSA in the range of 20.1- 100 ng /ml range was seen in 46.6% cases of carcinoma. Also 16.6% (5 out of 30) cases of carcinoma showed PSA in the grey zone.

Conclusion: Serum PSA levels when more than 20 ng /ml point towards carcinoma many cases of BPH can show values in the grey zone area that can cause unnecessary anxiety in patients. TRUS biopsies are useful for diagnosing prostatic adenocarcinoma.

Keywords: Carcinoma prostate, BPH, Serum PSA, Grey zone, TRUS biopsies.

Introduction

Incidence of carcinoma of prostate has gradually increased worldwide since the last fifty years due to the availability of better diagnostic techniques, widespread use of serum prostate specific antigen testing, increased life expectancy and awareness of the population in general.(1)

Among the male population, carcinoma of prostate is the second most common cancer and it stands at sixth place as a cause of cancer death worldwide.(2)

In India too carcinoma of prostate is the second leading cause of cancer among males in large metropolitan cities like Delhi and Kolkata and third leading cancer in Bangalore and Mumbai. According to the population based cancer registries in India it is among the top ten cancers in males. Prostatic cancer prevalence rate is more or less similar all over India. It is thought that the number of cases of prostatic cancer will double by the year 2020.(3) Hariharan et al(4) have observed wide variation in the incidence of prostatic cancer in different parts of our country. But they agree that the overall incidence is definitely less than the incidence in western population and that this malignancy is on the rise in India. Whenever carcinoma

of prostate is suspected clinically, a digital rectal examination (DRE), serum PSA testing, and biopsy of the prostate are performed.[5]

Ours being a tertiary care centre, we get patients of symptomatic prostatomegaly from neighbouring rural areas who are referred by physicians or surgeons for the TRUS guided biopsy procedure. As many of the cases are referral patients, their digital rectal examination findings; and serum PSA level in some cases are not available. In the present study we attempted to correlate the serum PSA levels with the histopathology on TRUS guided prostate biopsies.

Aim of the study

To study the histopathology of prostate biopsies and to correlate the serum PSA levels with biopsy findings of carcinoma and BPH and to study the biopsy findings for those cases with serum PSA in the grey zone area.

Materials and Methods

The present study was a retrospective study carried out in the department of Pathology at Kamineni Academy of Medical Sciences and Research Centre, Hyderabad, over a period of three years from January 2013 to December 2015. In this period a total of 128 TRUS biopsies were received out of which only 61 cases had undergone simultaneous serum PSA testing in our hospital in the department of Biochemistry. The study group consisted of these 61 cases. The patient age ranged from 40 to 79 years.

Inclusion criteria:

Cases of prostatomegaly who underwent TRUS guided prostatic core biopsy.

Only those cases were included for which simultaneous prebiopsy serum PSA testing was performed in our laboratory.

Exclusion criteria:

1. Cases who underwent only TRUS biopsy without serum PSA testing.
2. Serum PSA was tested after the biopsy procedure.
3. Serum PSA values were tested at other laboratories.
4. Histopathology specimens received as transurethral resection of prostate (TURP) were exluded.
5. Known cases of carcinoma of prostate on treatment undergoing repeat TRUS biopsies were excluded.
6. Recent history of instrumentation.

The TRUS (transrectal ultrasound) guided biopsies were carried out in the Radiology out-patient unit. Patients on antiplatelets or anticoagulants were reviewed by their primary care physician or cardiologist for stopping the drug 5 to 6 days prior to the procedure. A prophylactic broad spectrum oral antibiotic was given to all the patients prior to the procedure. The procedure was carried out in the left lateral decubitus position under local intrarectal lidocaine gel application. A spring biopsy device (biopsy gun) with 18 G needle was used. On an average, 6 to 12 core biopsies were obtained from each patient and especially any suspicious areas as seen on ultrasound were thoroughly sampled. The tissue cores were put in 10% buffered formalin fixative and were sent to the department of Pathology. All the biopsies were subjected to routine tissue processing. Five micron thick sections were cut and stained with hematoxylin and eosin (H and E) and examined under the microscope.

The pre-biopsy serum prostate specific antigen (PSA) levels of all the patients were retrieved from the department of Biochemistry. The serum PSA for all the patients was tested on Beckman Coulter Access 2 instrument based on the method of Chemiluminescence (CLIA).

The biopsy and serum PSA levels were analyzed.

Observations and Results

Table 1: Histopathological diagnosis of TRUS guided biopsies

Histopathologic categories	No. of cases	Percentage
Adenocarcinoma (Ca)	30	49.18
Suspicious of malignancy	03	4.91
Benign nodular	04	6.55

hyperplasia with focal atypia		
Benign nodular hyperplasia (NH)	24	39.34
Total	61	100

Out of total 61 cases, adenocarcinoma was reported in 49.18% and benign nodular hyperplasia in 39.34% cases. Perineural infiltration was present in 13 (43.3%) cases of adenocarcinoma.

Table 2: Age wise distribution in relation to histopathology

Age	Carcinoma	Suspicious of malignancy	Nodular hyperplasia with focal atypia	Nodular hyperplasia	No. of cases	Percentage (%)
40 - 49	3	0	0	0	3	4.9%
50 -59	3	1		7	11	18.0%
60 - 69	11	2	3	09	25	40.9%
70 - 79	10	-	1	6	17	27.8%
80 - 89	3	-	-	2	5	8.1%
Total	30	3	4	24	61	100%

Most number of patients indicated for TRUS biopsy and alco of adenocarcinoma and BPH were in the 60 to 80 year age range. The mean age for carcinoma and BPH was 66.5 and 66.4 years respectively.

Table 3: Histopathological categories and Serum PSA levels (ng/ml). N= 61

Histopathology	< 4	4 - 10	10.1- 20	20.1 - 100	> 100	Total no. of cases
Carcinoma	0	5	7	14	4	30
Suspicious of malignancy	0	2	1	0	0	03
Nodular hyperplasia with atypia	0	1	2	1	0	04
Nodular hyperplasia	1	9	6	8	0	24

For 46.6% (14 out 30 cases) of carcinoma prostate, and 33.3% (8 out of 24 cases) of BPH, the serum PSA levels were in the 20.1- 100 ng /ml range.

13.3% (4 out of 30) cases of carcinoma had serum PSA more than 100 ng/ml, whereas, none of the BPH cases had serum PSA more than 100 ng/ml.

A total of 17 (27.8%) cases had serum PSA in the grey zone of 4-10 ng/ml.

The mean PSA for carcinoma was 48.7 ng/ml. Carcinoma cases, 16.6% (5 out of 30) showed PSA in the grey zone.

Table 4: Gleason score in carcinoma prostate (n=30)

Gleason score	No. of cases	Percentage (%)
3+3	3	10%
3+4	19	63.3%
3+5	2	6.6%
4+3	1	3.3%
4+5	1	3.3%
5+4	2	6.6%
5+5	2	6.6%
Total	30	100%

A Gleason score of 3+4 was the most common score and was seen in 63.3% cases.

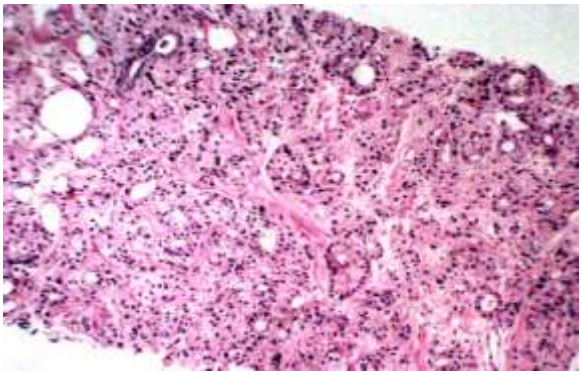

Fig. 1: Trucut biopsy of carcinoma prostate with Gleason score of 3+4. (Hematoxylin and eosin stain, 100 X)

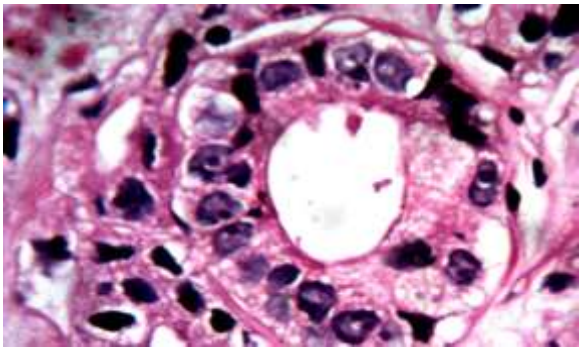

Fig 2: Trucut biopsy of carcinoma prostate with pleomorphic vesicular nuclei and prominent nucleoli in the glandular cells. (Hematoxylin and eosin stain, 400 X)

Discussion

The incidence of carcinoma of prostate in Indian population is less as compared to the Western population. However, this malignancy is being increasingly detected in India especially in the urban population.[4] In the present study 61 cases of prostatomegaly who underwent TRUS guided biopsies were studied and their serum PSA levels were correlated with the histopathology reports.

Manual and TRUS biopsy: Biopsy of the prostate can be performed with or without ultrasound guidance.[6] Carter et al. Digitally guided biopsies may miss localized lesions as it is a blind procedure. The guided biopsies are better and yield representative material in most of the cases. Lippman et al[7] also reported higher rate of detection of malignancy in prostate by the TRUS guided biopsy as compared to digitally guided biopsy. As ours is a tertiary care centre, all the biopsies were TRUS guided biopsies.

Age: In the present study, the mean age of prostatic carcinoma was 66.5 years. This compares well with the findings of Hariharan et al,[4] and Malathi et al,[8] Ganesh et al,[9] and Ghagane et al[10] who reported the mean age in their studies as above 65years, 65, 64, and 70 years respectively.

Serum PSA levels in BPH and PC: Serum PSA is the most accurate of the three diagnostic tests evaluated. The addition of DRE and TRUS improves the detection rate of prostate cancer over PSA alone.[11] However, other workers like Neal et al have concluded that PSA is not a suitable test for prostate cancer as it does not meet most of the criteria for a good screening test. They have recommended its use to identify the disease in high risk groups only such as men with first degree relatives with prostate cancer.[12]

PSA has been widely used as a diagnostics tool in the screening for prostate cancer. PSA level varies with age and nomograms are available that are mostly applicable to western population. The PSA levels can vary in different ethnic groups. A study by Sin-Eng Chin et al[13] showed similar median PSA levels in the Chinese, Malay, and Indian ethnic groups in Singapore. They also observed that the PSA values correlated well with the age group of patients and that the mean values were lower than the corresponding level observed in the white population in the United States. Mochtar et al[14] observed in their study that the predictive values of PSA for detection of cancer of prostate were more or less similar to those in Western Countries. Malathi et al[15] studied the serum PSA in healthy South Indian males and suggested a reference value for the same. They observed lower serum PSA in their study population as compared to other populations globally.

Ganpule et al[16] also studied the serum PSA in a subset of Indian population from Gujarat and observed slightly lower serum PSA levels than the western population. Though serum PSA estimation is widely used for the early detection of prostate cancer, Dubey et al[17] do not favor using this test for screening of

prostate cancer in Indian males as the incidence of this caner is low in India.

Shah et al[18] in their study compared four ethnic groups in India and found that the free PSA levels correlated positively with the age of the patient, but not with the ethnicity.

Gupta et al[19] also observed that healthy Indian men have lower age-specific serum PSA ranges compared to certain other populations of the world. They also confirmed that serum PSA correlates well with advancing ages.

Agnihotri et al[20] in their study have recommended prostate biopsy in only those symptomatic men whose serum PSA level was more than 5.5 ng /ml and who had a negative DRE. Ghagane et al[10] also reported mean PSA level as 37.71ng/ml in prostatic carcinoma patients.

Malathi et al[8] in their 2006 study observed high serum PSA level in patients with BPH and adenocarcinoma of prostate as compared to healthy males. In our study also 46.6% cases of carcinoma prostate and 33.3% cases of BPH showed an elevated serum PSA in the 20.1- 100 ng /ml range. Serum PSA can be elevated in non-carcinoma conditions such as BPH, prostatitis, infarcts of prostate, prostatic massage and prostatic biopsy.[21] Markedly elevated serum PSA, above 100 ng/ml points towards carcinoma of prostate. In our study, 13.3% cases of carcinoma had serum PSA more than 100 ng/ml, whereas, none of the cases of BPH had such high levels.

Malathi et al[8] in their study have reported mean PSA concentration as 3.6 ng /ml and the maximum PSA concentration as 28 ng /ml in patients of BPH. In our study the mean PSA and the maximum PSA for the BPH group was 17.6 ng /ml and 31 ng /ml respectively. Stamey et al. (1987)[21] also reported a maximum PSA concentration of 37 ng /ml in patients of BPH. The adenocarcinoma group in the study by Malathi et al[8] showed a mean PSA concentration of 408 ng /ml, and minimum and maximum PSA values in the carcinoma group as 10 and 9800 ng /ml respectively, whereas, in our study the mean PSA for carcinoma was 48.7 ng /ml and the minimum and maximum PSA values in the carcinoma group were 5.2 ng /ml and 155 ng /ml. In BPH patients from different countries the mean values reported for PSA are 7.9, 2.1 and 9.8 ng /ml.[21,22,23]

Several studies from different populations have documented varied percentage of patients having serum PSA concentration in grey zone area i.e. 4 to 10 ng/ml, for eg., 46%, 18%, and 31%.[23,24,25] In our study we observed that 27.8% cases had serum PSA level in the grey zone. In our study 37.5% patients of BPH had serum PSA in the universally accepted grey zone of 4-10 ng/ml and this compares well with the observation of Malathi et al[8] where 20.8% cases of BPH had serum PSA value in the grey zone. The PSA values beyond upper limit of grey zone i.e., 10 ng/ml were reported as 7% and 14% by Partin et al and Barak et al.[23,26] However, several studies reported only 2-3% of BPH patients to have PSA greater than 10 ng/ml.[25] The study by Malathi et al[8] revealed 8.2% BPH patients to have PSA greater than 10 ng/ ml. In our study 58.3% of patients of BPH (14 out of 24) had serum PSA level more than 10 ng /ml. Most of them on biopsy showed concomitant acute inflammation too which could have contributed to the rise in serum PSA. These patients were advised follow up PSA estimation. However, transient rise and fluctuating concentration of PSA is suggestive of benign disease of prostate.[8]

It has been shown that some men with PSA levels less than 4.0 ng /ml have prostate cancer and that many men with higher levels do not have prostate cancer.[27]

Table 5 shows comparison of serum PSA in cases of BPH and carcinoma in our study with that of other studies.

Table 5: Comparison of serum PSA in BPH and prostatic carcinoma with other studies

Study	Serum PSA in BPH (ng/ml)	Serum PSA in Carcinoma (ng/ml)	% of cases with BPH having serum PSA in Grey zone
Present study	3.2-31	5.2-155	37.5%
Malathi et al[8]	0-28	10-9800	20.8%
Amayo et al[28]	0.34-36	1.78-4339	29.6%
Naz et al[29]	3-24	3.2-80.6	50%
Shetty et al[30]	0.4-4.6	10-1525	45%
Akhter et al[31]	-	3.15-4240	30%

Histopathological findings: In the present study, carcinoma was seen in 49.1% cases similar to the findings of Hosein et al[32] who encountered carcinoma in 51.8% cases out of 546 patients studied.

Kanya Kumari et al[33] (n=70) observed 44.28% cases with adenocarcinoma, and 20% having benign prostatic hyperplasia.

A Gleason's score of 6 was seen in 10% patients. A score of 7 was the commonest and was seen in 20 (66.6%) patients. In a study by Ghagane et al[10] the most common score was ≥8 seen in 88.7% cases. They also found significant positive correlation between serum PSA level and Gleason score. Other authors[32] have reported Gleason's score 7 as the commonest score in prostatic carcinoma. In a study by Kanya Kumari et al[33] also the most common Gleason score was reported as 7 (3+4) and was found in 51.61% of patients. In our study we observed perineural infiltration in 43.3% cases. Bismar et al[34] observed 11% perineural infiltration in prostatic carcinoma in their study. Presence of perineural infiltration is considered a poor prognostic factor.

Conclusions

Carcinoma of prostate is more common in men above 65 years. The serum PSA levels are helpful in pointing towards carcinoma when they are higher than 20 ng /ml. Cases of BPH can show PSA values in the grey zone area that can cause unnecessary alarm in patients. Both urologic and non-urologic clinicians need to be aware of this so as to allay the anxiety in patients till the final TRUS biopsy report is available.

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