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Research Paper

Histopathological lesions in Transrectal ultrasound guided biopsies of Prostate in patients with raised serum Prostate specific antigen

Pathology

KEYWORDS : Transrectal ultrasound (TRUS), Benign Prostate Hyperplasia, Serum Prostate Specific Antigen (PSA), Adenocarcinoma.

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ABSTRACT

Introduction: Carcinoma of Prostate is one of the common tumors of old age in men. With digital rectal examination (DRE), Prostate specific antigen (PSA) and Transrectal ultrasound (TRUS)-guided needle biopsies of prostate are considered the gold standard for the diagnosis of the Prostatic cancer.

Objectives: To determine the spectrum of Pathological lesions in TRUS-guided needle biopsies of Prostate in men with increased serum Prostatic specific antigen (PSA) levels (≥4 ng/ml) with or without symptoms of Prostatism.

Patients and methods: A Retrospective study carried out at the Department of Histopathology, B.J.M.C and Civil hospital, Ahmedabad from January 2013 to November 2013. The study includes 108 cases between 50 to 76 years of age group. Serum PSA level and Histopathology of Prostatic biopsy was done and correlate.

Results: In present study ,out of 108 cases, 60 (55.6%) cases showed Benign lesions with mean age 57.7 ±4.86. and 48 (44.4%), Malignant with mean age 65.70 ± 5.64.The mean serum PSA value was 13.36 ± 8.6 ng /ml.

Conclusions: In present study, Elevated level more than 4.0 ng /ml with TURS guided needle biopsy is most useful and accurate diagnostic method for Prostate.

1.Introduction:

Prostatic carcinoma is an important growing health problem, presenting a challenge to urologists, radiologists and pathologist (1,2).Incidence of prostatic diseases, benign prostatic hyperplasia, and carcinoma increases with age.(3) Prostate cancer is the leading cause of new cancer in men and is second only to lung cancer as a leading cause of cancer-related deaths in men(4) .Several factors, including age, race, family history, hormone levels, and environmental influences are suspected to play a role in pathogenesis (5). This study includes description of incidence of various lesions of prostate, their clinical manifestations, serum prostate specific antigen (PSA) level, classification and grading of prostate tumors. The diagnosis requires careful history, physical examination including digital rectal examination (DRE), serum prostate specific antigen (PSA) estimation and transrectal ultrasound (TRUS) and TRUS-guided needle biopsies of the prostate. Among these, the latter are considered the gold standard for the tissue diagnosis of the prostatic cancer. To correlate the serum PSA level findings with histopathological diagnosis (6).

2. Aims and Objective:

- To determine the age distribution of patients with prostatic lesion.
- To study prevalence of distribution of various prostatic lesions, admitted in Civil hospital, Ahmedabad.
- To determine histological types related with prostate specific antigen.

3. Patients and Methods:

3.1. Patients

A Retrospective study carried out at the Department of Histopathology, B.J.M.C and Civil hospital, Ahmedabad from January 2013 to November 2013. The study includes 108 cases between 50 to 76 years of age group, who presented to with or without complaints of prostatism. Their detailed physical examination and DRE were performed, followed by appropriate laboratory investigations including determination of serum PSA. Serum PSA levels were calculated and correlated with various clinical and biopsy findings.

3.2. Biopsy technique

TRUS guided needle biopsies of the prostate gland were performed only in those patients who had serum PSA levels ≥ 4ng/ml and/or abnormal DRE suspicious for prostate cancer. Ultrasound guidance was provided by a diagnostic ultrasound machine with, biplanar transrectal probe. Biopsies were obtained with patient in right or left lateral decubitus position and the prostate was imaged in the sagittal plane (7,8). Only first time biopsies were included. Repeat biopsies were not included in the analysis.

3.3. Pathologic study

The biopsy specimens were processed and studied at the department of Histopathology, B.J.M.C. Gross examination of the biopsies included precise length and diameter and colour of the cores. The biopsies were processed for paraffin embedding, cut at 3-5 um and stained by haematoxylin and eosin (H&E) for detailed microscopic examination.

The histopathological grading and scoring by Gleason system was done in all cases of adenocarcinoma of prostate. Demographic, clinical and laboratory data of each patient was taken from the clinical charts. Histopathological features were noted from original biopsy reports. The grading system for prostate carcinoma devised by Gleason was used. The primary and secondary patterns were combined to give a tumour score, referred to as Gleason score (9). The core biopsies were graded and scored according to revised WHO criteria for the grading and scoring of needle biopsies of the prostate (10).

3.4. Statistical analysis

Simple descriptive statistics such as mean ± SD were used for continuous variables such as age and clinical and laboratory parameters. Percentages were used for categorical data. For comparisons of prostate cancer and the non-cancer group, independent-samples T test and Chi - square tests were used. A p value of less than 0.05 was considered significant.

4. Results: The main clinical features of all patients are shown in (Table-1). in variable combination. Overall 99 (92%) patients were symptomatic at the time of presentation.

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Table: 01- Main presenting symptoms of the patients

Sr. No.	clinical features	No. of cases(%)
1	Retention of urine	40(37.0%)
2	Weak stream	36(33.3%)
3	Frequency	30(27.7%)
4	Urgency	18(16.6%)
5	Hematuria	14(12.9%)
6	Nocturia	12(11.1%)
7	Hesitancy	08(7.4%)

In present study, The Mean age of all patients 63.9 ± 9.5 years. out of 108 cases, 60 (55.6%) cases showed benign lesions with mean age 57.7 ± 4.86 years and 48 (44.4%) Malignant with mean age 65.70 ± 5.64 years.(Table-2).

Table: 02- Age wise distribution of cases.

Sr. No.	Age range (years)	Benign lesion No. of cases(%)	Malignant lesion No. of cases(%)
1	50-60	20(33.3%)	16(33.3%)
2	61-70	30(50.0%)	20(41.7%)
3	› 70	10(16.7%)	12(25.0%)

In most cases (79.6%), eight cores were obtained. Minimum number of cores obtained per case was 4 and maximum 9 (7,8).

Out of 108 cases, 48 (44.4%) revealed adenocarcinoma and the remaining 60 (55.6%) showed adenomyomatous hyperplasia (figure-2) with or without associated active prostatitis (figure-3) (Table-3).The six patients with chronic granulomatous inflammation showed no caseation necrosis and negative results for acid fast bacilli on Ziel-Nelson staining and thus were labeled as idiopathic granulomatous prostatitis.(figure-4).

Table: 03 - No. of cases according to histopathology diagnosis

Sr. No.	Histopathological Diagnosis	No. of cases(%)
1	Adenocarcinoma	48(44.4%)
2	BPH	28(29.92%)
3	Chronic non specific Prostatitis	12(11.1%)
4	Acute ;Prostatitis	6(5.55%)
5	PIN	3(2.77%)
6	Chronic Granulomatous Prostatitis	6(5.55%)
7	Others (foreign body granuloma,Non specific)	5(4.62%)

The mean serum PSA value was 13.36 ± 8.6 ng/ml; total range was 4 to 36 ng/ml. The mean PSA was significantly higher in the cancer group (p, 0.001) than in the benign. The rate of cancer detection increased significantly with increasing serum PSA level. 28 out of 108 patients (25.9%) had serum PSA ≥ 20.1 ng/ml. Of these, 24 (85.7%) patients had prostatic adenocarcinoma, and 4 (14.3%) benign changes(Table no-4).

Table: 04 -Histopathology diagnoses related with Mean PSA level

Sr. No.	Histopathological Diagnosis	MEAN PSA LEVEL (ng/ml) [MEAN ± SD]
1	BPH	6.16 ± 2.4
2	Adenocarcinoma	24.635±9.4
3	Prostatitis	4.36±3.59
4	PIN	9.26 ± 4.34

Out of 108, 60 (55.6%) showed adenomyomatous hyperplasia with or without associated active prostatitis. Among 48 patien- with adenocarcinoma, according to Gleason's grading system, 12 patients (25%) had grade 3, 22 (45.83%) grade 4 (Figure 1) and remaining 14 (29.1%) patients had grade 5. Most of the patients having grade ≥ 3 showed markedly high levels of serum PSA. Similarly, on Gleason scoring, eight patients (16.67%) had score 6, twelve (25.0%) score 7, ten (20.83%) score 8, fourteen (29.1%) score 9 and four (8.33%) had score 10 (Table no- 5). Most of the patients having Gleason score ≥ 6 also showed markedly high levels of serum PSA.

Table:5- Histopathological characteristics of prostate cancer observed in 48 patients with raised serum prostate specific antigen levels.

Patients	[No. of cases (%)]
Biopsy Gleason grade	
3	12(25.0)
4	22(45.83)
5	14(29.1)
Biopsy Gleason score	
6	8(16.67)
7	12(25.0)
8	10(20.83)
9	14(29.1)
10	4(8.33)
Positive biopsy cores	
1	6(12.5)
2	2(4.2)
3	4(8.3)
4	4(8.3)
5	6(12.5)
6	22(45.8)
8	4(8.3)

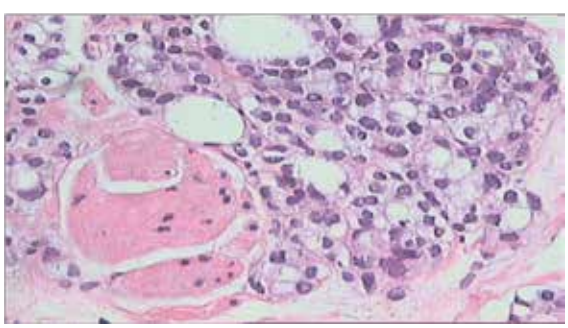

Figure -1: High magnification image showing a few glandular lumina with focal areas of loss of glandular differentiation, a pattern consistent with Gleason grade 4 adenocarcinoma of the prostate (H&E, × 400).

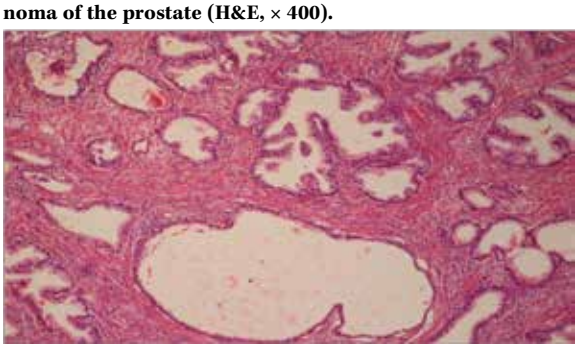

Figure-2: Benign prostatic hyperplasia with glandular and stromal proliferation and dilated gland (H & E, 100X)

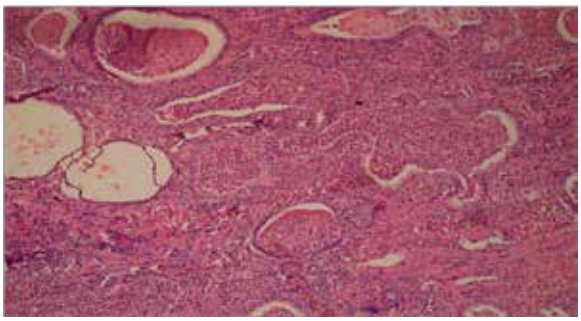

Figure-3: Chronic prostatitis showing infiltration of lymphocytes, plasma cells, histiocytes in the stroma and secretions and neutrophils in lumen (H & E, 100X)

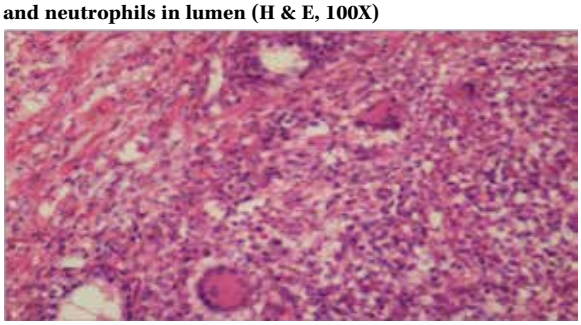

Figure-3: Granulomatous prostatitis showing epitheloid cell granulomas and giant cells (H & E, 400X)

5. Discussion: Carcinoma of prostate is common cancer in India due to increasing life expectancy and relatively better diagnostic method. The gold standard triad for diagnosing prostate cancer comprised DRE, PSA level and Transrectal ultrasonography (11).

The prostate cancer is seen typically in elderly men and its frequency rises with increasing age (5). In this context, the mean age of our patients is concordant with that reported previously in local and international studies (12). However, significant rise in cancer incidence was seen in our patients with increasing age, as in other studies (5).

In our study, most patients were symptomatic; 92% presented with lower urinary tract symptoms (LUTS) commonly known as prostatism. Very few patients (8%) presented for screening of the prostate cancer at asymptomatic stage.

The overall cancer detection rate in TRUS-guided biopsies in our series was 44.4%. This corresponds fairly well with many previously reported series from around the world (12). In a study from China, cancer detection rate was 40% (6). In the study by Levine et al. (13) cancer was detected in 31% of cases. Presti et al. observed prostate cancer in 42% of the TRUS-guided biopsies (14). All these studies included patients with raised serum PSA associated with or without prostatism, as in our study.

The proportion of benign lesions was greater in patients with mild or moderate elevations of serum PSA. In contrast, cancer was more frequent in cases with marked elevations in serum PSA. Similar observations have been noted in previous investigations as well. These findings show that simply a rise in serum PSA levels ≥ 5 ng/ml does not indicate that a patient has prostate cancer because benign conditions such as hyperplasia and prostatitis can also increase the serum PSA levels (15,16). In our study, 28 (25.9%) patients had PSA levels of ≥ 20 ng/ml, of which 24 (85.7%) patients had adenocarcinoma,4(14.3%) patients had hyperplasia; one of the later had active prostatitis also.. This is an interesting finding which shows that patients with markedly elevated serum PSA levels are more likely to harbor adenocarcinoma in their biopsies than benign changes, as in previous studies (6)(table-6).

It was observed that the levels of serum PSA increased with increasing Gleason grade and score of the tumour. In our study, majority of cancers (44/48: 91.6%) belonged to intermediate to high grade category. Similarly, scores were also moderate to high in majority of cases. Most of the patients having grade 3 or above showed markedly high levels of PSA.

Table : 06:- Benign and malignant Prostatic lesion: Comparison between PSA level with other study.

PSA Range	Benign Prostatic hyperplasia			Malignant prostatic lesion			
Ng /ml	Kshitijet al18	Ishtiaq Ali Khan etal19	Presentstudy	Kshitijet al18	H.A Mwalyoma et al19	Sladana Zivkovic et al20	Presentstudy
0-4	71.6%		-	10.5%		2.50%	-
4-10	22.6%	85%	87.6%	26.3%	5.3%	27.50%	14.9%
>10	3.0 %	15%	12.4%	63.7%	94.7%	70.0%	74.2%

Table:06- shows cases of BPH most commonly present between PSA level 4-10 ng/ml (87.6%), which is compared with study of Khitij et al. and cases of Adenocarcinoma is more commonly present at PSA level >10.0 ng/ml (74.2%) and it is compared with other study.

6.Conclusion: In present study, the commonest pathology encountered in the TURS guided prostate biopsy was Benign lesion (55.6%). Incidence of carcinoma was 44.4%.60 (55.6%) cases showed benign lesions with mean age 57.7 ±4.86. and 48 (44.4%) Malignant with mean age 65.70 ± 5.64. The mean serum PSA value was 13.36 ± 8.6 ng/ml. the mean serum PSA was 24.635±9.4 ng/ml in adenocarcinoma, In Benign prostatic lesion mean serum PSA level was 6.16 ± 2.4 ng/ml. In present study serum PSA level are the most useful front line methods for assessing and individual's risk of prostate cancer. In addition elevated level more than 4.0 ng/ml with TURS guided needle biopsy is most useful and accurate diagnostic method for prostate. The detection rate of prostate cancer is almost similar to that reported previously in literature with similar biopsy indications from different parts of the world.

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