Research Article

Analysis of prostatic biopsies in a tertiary care hospital in correlation with prostate-specific antigen levels: A clinicopathological study

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ABSTRACT

Background: Benign prostatic hyperplasia (BPH) and adenocarcinoma account for considerable morbidity in aging men. Prostate-specific antigen (PSA) is a useful biomarker in the diagnostics along with digital rectal examination and transrectal ultrasonography. **Objective:** To analyze various clinicopathological features in benign and malignant prostatic lesions and correlate the histologic findings with pre-operative PSA level for confirmation of diagnosis in cases with a diagnostic dilemma. **Material and Methods:** The study included 112 prostatic tissue specimens received in the Department of Pathology, Smt. NHL Municipal Medical College, Ahmedabad, Gujarat, over the period of 2-year from October 2014 to September 2016. Relevant clinical data and serum PSA value was recorded, and Gleason's microscopic grading was used to grade malignant lesions. **Results:** Mean age of presentation was 66.5 ± 10.67 years with maximum incidence in the seventh decade of life. BPH (68.79%) was the most common lesion followed by adenocarcinoma (25%). Other lesions encountered were Prostatitis (2 cases), high-grade prostate intraepithelial neoplasia (2 cases), adenosquamous carcinoma (1 case), atypical small acinar proliferation (1 case), and retention cyst (1 case). The most common Gleason score was score 7 (55.17%) followed by score 9 (10.34%) and score 6 (6.9%). Pattern 4 was most common predominant pattern. Serum PSA level was correlated in benign and malignant lesions. **Conclusion:** With increasing awareness and life expectancy in the current era, histopathological evaluation of prostatic biopsies is mandatory to avoid pitfalls in clinical diagnosis aided by serum PSA assay and other investigations.

KEY WORDS: Benign prostatic hyperplasia; Adenocarcinoma; Prostate specific antigen

INTRODUCTION

Benign prostatic hyperplasia (BPH) and prostatic adenocarcinoma are very frequent prostatic diseases in elderly men in their sixties and responsible for considerable morbidity and mortality.[1] Prostate cancer is the second most frequently diagnosed cancer in men and the fifth most common cancer overall in world population.[2] Furthermore, prostate is the second leading site of cancer among males according to national cancer registries in India.[3] Both BPH and carcinoma of prostate show parallel rise in incidence with advancing age.[4] Based on histological architecture of prostatic tumor Gleason developed a grading system for prostate carcinoma.[5] Many modifications took place since then.[6] The currently popular system for the Gleason's score (GS) was accepted in "The 2005 international society of urological pathology (ISUP) consensus conference on Gleason grading of prostatic carcinoma" held to standardize the score. The result of this consensus was the exclusion of Gleason's pattern 1 in diagnosing prostate carcinoma, the near extinction of pattern 2 and some modifications in the diagnostic standards of pattern 3, 4 and 5.[7] Measuring of serum prostate specific antigen (PSA) level is the first line screening tool for prostate carcinoma along with digital

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rectal examination (DRE).[8] The upper limit of normal for PSA values is generally considered to be 4.0 ng/mL; between 4 and 10 ng/mL is considered borderline and more than 10 ng/mL is considered high. PSA value of 4 ng/mL is considered cutoff because of its high sensitivity (detection of the largest number of prostate cancers) and high specificity (exclusion of the greatest number of men without prostate cancer).[9] The Gleason score and prostate-specific antigen (PSA) level are the most important prognostic factors in prostate cancer. However, the definitive Gleason score can only be obtained after radical prostatectomy (RP).[10] The purpose of this study is to analyze various clinicopathological features in benign and malignant prostatic lesions and to correlate histologic findings with pre-operative serum PSA levels for confirmation of diagnosis in cases with diagnostic dilemma.

MATERIALS AND METHODS

This prospective study was conducted from October 2014 to September 2016 in the Department of Pathology, Smt. NHL Municipal Medical College, Ahmedabad, Gujarat, India, on patients who had clinical symptoms of prostatism. A total of 112 prostatic biopsy specimens were received included simple and RP, Transurethral resection of prostate (TURP) and Trucut biopsies. Inadequate biopsies were excluded. Relevant clinical data of each patient about age, presenting symptoms, and provisional clinical diagnosis were collected from indoor case papers and biopsy requisition forms. Serum PSA level (total PSA assay) of all patients was done on Abbott ARCHITECT Ci 4100 Analyzer by by Chemiluminescent microparticle immunoassay. Biopsies were fixed in 10% formalin. Routine paraffin processing of tissue and hematoxylin and eosin staining was done. In cases of Trucut biopsies, all the tissue received was fixed and processed. In cases of TURP chips 3-4 cassettes were prepared in each case, which accommodated approximately 50% of total tissue, and weighed approximately 9-12 g; specimens weighing <12 g were submitted entirely. In case of prostatectomy specimens, multiple sections were made at the distance of 3-5 mm; the slice in which tumor appears closest to the resection margin was submitted entirely after dividing into an adequate number of sections. Special stains like ZN were performed whenever necessary. Histomorphological findings of the lesions were analyzed. The Gleason grading system was used to grade adenocarcinomas. All the data were subjected to statistical analysis by simple interactive statistical analysis.

RESULTS

A total of 112 specimens were received during the study period in which Trucut biopsies constituted the major bulk (60 cases-53.6%), followed by prostatectomies (28 cases - 25%) and TURP chips (24 cases - 21.4%). Mean age of presentation with prostatic disorders was 66.5 ± 10.67 years with mean age in BPH cases was 65.07 years and 71.03 years in carcinoma cases. A maximum number of patients (35.72%) was in the seventh decade. Benign lesions were more common in age group of 60-69 years, and malignant lesions were more common in age group of 70-79 years (Figure 1). Frequency of urination was most common presenting symptom (48 cases - 25%) followed by difficulty in voiding (38 cases - 20%) (Figure 2). The most common histopathological diagnosis was BPH (77 cases - 68.75%) followed by acinar adenocarcinoma (28 cases - 25%). Two cases of chronic nonspecific prostatitis, one case of benign cystic lesion-retention cyst, one case of atypical small acinar proliferation, two cases of high grade prostatic intraepithelial neoplasm (HGPIN), and one case of adenosquamous carcinoma were also encountered while evaluating the biopsies (Figure 3). Out of 77 cases of BPH 30 cases (26.78%) had associated chronic prostatitis, and one out of them was granulomatous prostatitis (acid-fast bacilli positive). The most common Gleason score given in adenocarcinoma cases was score 7 (16 cases - 55.17%), followed by score 8 (8 cases - 27.6%), score 9 (3 cases - 10.34%) and score 6 (2 cases - 6.9%) (Table 1). Adenosquamous carcinoma had score 7 (4+3). Pattern 4 was

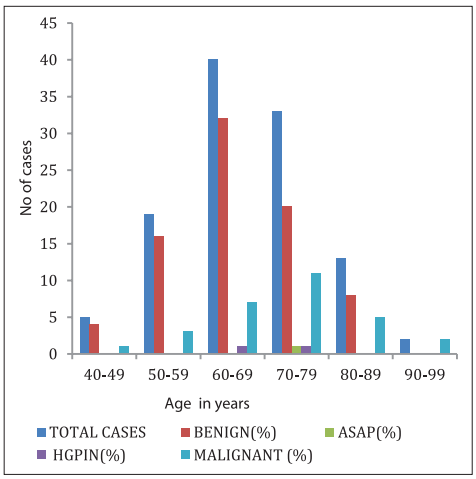

Figure 1: Age distribution: Prostatic lesions

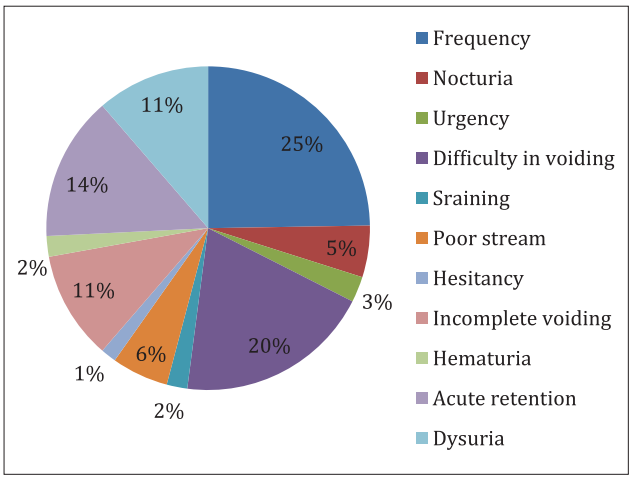

Figure 2: Clinical presentation

the most common predominant pattern (16 cases - 55.17%) followed by pattern 3 (11 cases - 37.93%) and pattern 5 (2 cases - 6.89%). Pattern 1 and 2 were not found in biopsies. Perineural invasion was seen in 7 (24.13%) cases out of 29 prostate carcinoma cases; among these three cases had Gleason score 7 and four cases had Gleason score 8. BPH cases had mean PSA level of 5.02 ± 3.13 ng/ml with normal level (<4 ng/ml) found in 44 (57.14%) cases; mild elevation (4-10%) was seen in 18 (23.37%) cases; modest elevation (10.1-20 ng/ml) was seen in 11 (14.28%) cases; marked elevation of PSA (>20 ng/ml) was seen in 4 (5.19%) BPH cases. Adenocarcinoma cases had mean PSA level of 60.63 ± 38.42 ng/ml with mild elevation seen in 3 (10.71%) cases; modest elevation in 4 (10.28%) cases and marked elevation was seen in 21 (75%) cases out of which 15 cases had PSA level of >80 ng/ml. Prostatitis cases showed mean PSA level of 31.8 ± 39.03 ng/ml and HGPIN cases had mean PSA level of 15.5 ± 7.78 (Table 2).

Table 1: Analysis of adenocarcinoma cases by GS

GS	Number of cases*	Total cases (%)
6 (3+3)	2	2 (6.89)
7 (3+4)	8	16 (55.17)
7 (4+3)	8	
8 (4+4)	7	8 (27.60)
8 (3+5)	1	
9 (4+5)	1	3 (10.34)
9 (5+4)	2	
10 (5+5)	0	0
Total	29	29 (100)

*One case was of adenosquamous carcinoma: 7 (4+3).
GS: Gleason's score

Table 2: Histopathology diagnoses related with mean PSA level

HP diagnosis	PSA level (mean±SD)
BPH	5.02±3.13
Adenocarcinoma	60.63±38.42
HGPIN	15.5±7.78
Prosatatitis	31.8±39.03

PSA: Prostate specific antigen, HGPIN: High grade proastatic intraepithelial neoplasm, BPH: Benign prostatic hyperplasia

DISCUSSION

BPH and carcinoma prostate are very common companions of men in geriatric age causing various types of obstructive urinary symptoms. DRE, transurethral ultrasonography, raised PSA level, and needle biopsy/Trucut needle biopsy are a standard protocol used to reach the final diagnosis.[11] Mean age of the patient was 66.5 years with mean age of BPH being 65.07 and adenocarcinoma 71.03 years. Maximum (35.7%) patients were in the seventh decade with benign lesion more common in age group of 60-69 years and malignant lesion in age group of 70-79 years. No case was found below the age of 40. These findings are similar to various studies on prostatic lesions such as Jasani et al.,[12] Anushree et al.,[13] Aslam et al.,[14] and Akhtar et al.[15] Frequency of urination was most common presenting symptom followed by difficulty in voiding suggesting urethral constriction by prostatic enlargement; similar finding was also observed in Akhtar et al.[15]

BPH was the most common histopathological diagnosis followed by adenocarcinoma similar to other studies mentioned above. Chronic prostatitis was associated with one-fourth (26.78%) of BPH cases similar to Josephine et al.[4] (25.31% cases).

The Gleason grading of prostatic carcinoma correlates with tumor aggressiveness, tumor volume, serum PSA levels, prognosis, and influence of the treatment policy.[4] In this study, the most common Gleason score was score 7 and the most common predominant Gleason pattern was pattern 4 followed by pattern 3 and 5. These findings were also observed in Deshmukh et al.,[16] Shirish et al.,[1] and Josephine et al.[4] In the study done by Kansal et al.,[17] 62.71% of patients had GS of 5-7; 13.55% had GS 8-10 and 23.72% with GS of 2-4. In the study done by Josephine et al.,[4] 60% of patients had GS of 5-7; 20.5% had GS 8-10 and 15% with GS of 2-4. While in this study, 62.1% of patients had GS of 5-7 and 37.9% of patients had GS of 8-10. GS 2-4 was not found in present study. This may be due to a larger number of Trucut needle biopsies received as compared to RP specimens. Perineural invasion was seen in 7 (24.13%) cases of prostate carcinoma cases; among these three cases had GS 7 and four cases had GS 8. Thus, perineural invasion was more common

Table 3: Analysis of prostatic lesions with range of PSA levels

PSA (ng/ml)	BPH (%)	Prostatitis (%)	Retention cyst (%)	HGPIN (%)	ASAP (%)	Adenocarcinoma (%)	Adenosquamous carcinoma (%)
<4	44 (57.14)	-	1 (100)	-	-	-	1 (100)
4-10	18 (23.37)	1 (50)	-	1 (50)	1 (100)	3 (10.71)	-
10.1-20	11 (14.28)	-	-	-	-	4 (14.28)	-
>20	4 (5.19)	1 (50)	-	1 (50)	-	21 (75)	-
Total	77 (100)	2 (100)	1 (100)	2 (100)	1 (100)	28 (100)	1 (100)

PSA: Prostate specific antigen, HGPIN: High grade proastatic intraepithelial neoplasm, BPH: Benign prostatic hyperplasia, ASAP: Atypical small acinar proliferation

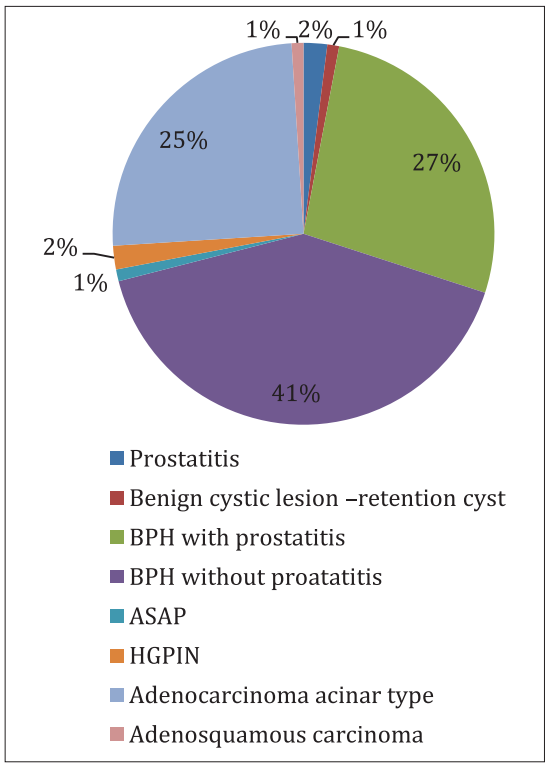

Figure 3: Histopathological spectrum of prostatic lesions

in patients with high GS which is comparable with Kansal et al.[17] (4 out of 6 patients having perineural invasion had GS of 8-10).

PSA is a useful biomarker for early diagnosis and monitoring of prostate cancer. Because of its less predictive efficiency in low and intermediate range and potential for the overdiagnosis of nonthreatening cancer, it is not used alone as a screening tool.[18]

Mean PSA level in BPH cases was 5.02 ± 3.13 ng/ml with normal level in 57.14%, mild elevation in 23.37%, modest elevation in 14.28%, and marked elevation seen in 5.19% cases in this study (Table 3). These findings are comparable to Jasani et al.[12] (mean PSA level - 4.86 ± 3.03; normal PSA level - 63.72% of cases, modest elevation - 27.4% of cases and marked elevation - 8.8% of cases). Modest elevation in BPH cases may be due to associated inflammation or infection leading to chronic or granulomatous prostatitis and abscess formation. Adenocarcinoma cases in this study had mean PSA level of 62.63±38.42 ng/ml with the majority of cases (75%) having marked elevation in PSA level; out of which 15 cases had PSA level of >80 ng/ml. One case of adenosquamous carcinoma showed lowest normal PSA level (0.0067 ng/ml) and one case of BPH showed marked elevation (100 ng/ml) which points to failure of PSA to predict the malignancy. Comparing PSA levels in BPH and adenocarcinoma cases, it was seen that with increasing PSA levels number of BPH cases decreases while number of adenocarcinoma cases increases (Figure 4).

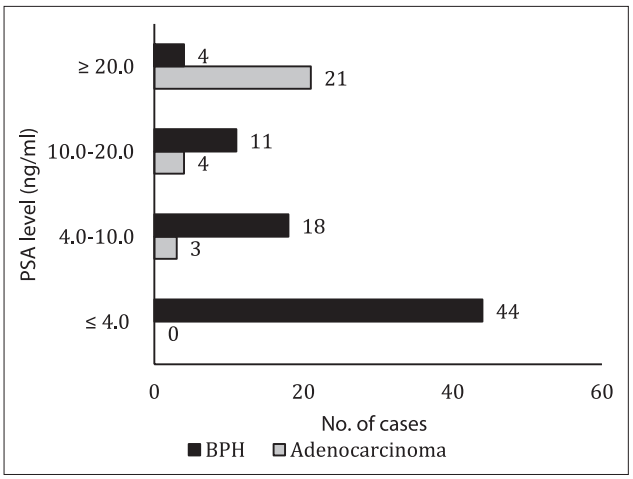

Figure 4: Comparison of prostate-specific antigen level in adenocarcinoma and benign prostatic hyperplasia cases

Limitation of our study was that sample size did not represent the whole population as it was based on patients of V.S general Hospital, Ahmedabad, Gujarat. Our study opens the door for further research and it should be continued in more advanced setting for better understanding of clinicopathological correlation of prostatic lesions.

CONCLUSION

Our study concluded that BPH was the most common lesion followed by adenocarcinoma in men with clinical symptoms of prostatism in their seventh decade of life. Perineural invasion is more common with high GS. Strong correlation of PSA level with adenocarcinoma was seen in our study; however, histopathological evaluation of prostatic biopsies is mandatory to avoid overdiagnosis of malignancy under high index of clinical suspicion with higher PSA level.

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