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Study of clinicomorphologic spectrum of prostatic lesions and correlation with prostate specific antigen levels in a tertiary care center

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Abstract

Introduction: Benign and malignant lesions of prostate are some of the commonest problem of elderly men age group. Prostate specific antigen level, histopathological examination, and digital rectal examination are considered three most important evaluation criteria.

Objective: To study clinical and histopathologic spectrum of prostatic lesions and compare prostate specific antigen levels in various non-neoplastic, benign and malignant lesions of prostate.

Materials and Method: Study was performed prospectively and retrospectively from January 2013 to December 2016 in the department of Pathology in the tertiary care centre in North Gujarat area over the span of 3 years. Histopathologically Gleason system scoring was analyzed. Prostate specific antigen value was noted in each case.

Results: Mean age of all 140 cases was 65.5± 10.7years, of all BPH cases it was 66.07 years, and 72 years of adenocarcinoma cases. Frequency of urination was most common presenting symptom (42 cases - 30%) followed by difficulty in voiding (38 cases – 27.14%). The commonest histopathological diagnosis was benign prostatic hyperplasia - 90 cases (64.28%), next is adenocarcinoma -38 cases (27.14%). The commonest Gleason system score in prostatic adenocarcinoma cases was score 7. Benign prostatic hyperplasia and Prostate carcinoma cases had mean prostate specific antigen value of 5.05 ± 3.15 ng per ml and 59.65 ±38.65 ng per ml respectively.

Conclusion: Prostate specific antigen value should be measured periodically in elderly men as a screening tool. Each higher value must be followed by histopathological evaluation of prostate biopsy for exact nature of disease confirmation.

Keywords: Prostate specific antigen, Benign prostatic hyperplasia (BPH), Prostate adenocarcinoma, Gleason score,

Introduction

Carcinoma prostate is an important health problem of elderly male population, and pose a challenge to urologists, radiologists and pathologists.[1,2] Currently, many men are identified as having early prostate cancer through the use of prostate specific antigen screening.[3-6] Carcinoma of the prostate is the most common malignant tumor in men over the age of 65years.[7] Carcinoma prostate is the most frequently diagnosed cancer in men next to carcinoma lung and according to national cancer registries in India it is the second leading site of cancer.[8,9] There is parallel rise in incidence with advancing age of BPH and prostate carcinoma.[10] Gleason developed a grading system for prostate carcinoma, based on histological architecture of prostatic tumor over the period, Gleason system has been modified thereafter from time to time.[11,12] Gleason pattern 1 has been excluded, pattern 2 is almost extinct and pattern 3, 4, 5 has been modified diagnostically as a result of international society of urological pathology conference consensus.[13]

Along with digital rectal examination, measuring of serum prostate specific antigen level is the first line screening tool for prostate carcinoma.[14] Up to 4.0 ng per mLPSA value is considered normal, between 4 to 10 ng per mL is considered borderline and more than 10 ng per mL is considered as high. 4 ng per mL value is the cut off range for prostate specific antigen because it has both higher sensitivity as well higher specificity (for detection of true positive as well exclusion of true negative).[15]

For the prognostic significance of patients with carcinoma of prostate, Gleason grading score and prostate specific antigen are the two most useful criteria. Radical prostate excision is the only measure to detect exact Gleason score.[16] Our study aims to show different clinical and histopathological features of prostate malignancy as well benignity and correlation of it with serum level of prostate specific antigen.

Materials and Method

Study was performed prospectively and retrospectively from January 2013 to December 2016 in the department of Pathology in the tertiary care center in north Gujarat area over the period of 3 years. Total 140 prostatic biopsies received were studied which included different biopsies namely simple prostatectomy, radical prostatectomy, trucut biopsies and transurethral resection of prostate. Clinical information of patients namely age, clinical symptoms, prostate specific antigen value as well clinical diagnosis made provisionally were collected from history sheets, indoor admission form, and request form for histopathology examination. 10% neutral buffered formalin is the fixative used for biopsies. After that biopsies grossed, and then put in automated tissue processor overnight. Then paraffin blocks were made and then tissue stained with hematoxylin and eosin on a glass slide. Trucut biopsies

were taken whole for section, in transurethral resection of prostate chips approximately 50% of the tissue weighing approximately 10 gram was taken for section. If the specimen contains less than 10 gram then it is whole processed. Total and partial prostatectomy specimens were grossed with sections at 4-5 mm distance, resection margin with tumors were processed entirely. Microscopical findings were analyzed. Grading was done with Gleason system of grading. All the data are statistically analyzed.

Results

Out of total 140 specimens received 84 cases were trucut biopsies (60%), 32 cases were prostatectomy (22.85%) and 24 were transurethral resection of prostate chips (17.14%). Mean age of all 140 cases was 65.5± 10.7years, of all benign prostatic hyperplasia cases it was 66.07 years, and 72 years of adenocarcinoma cases. Maximum patients were of age range 60-69(37%). Benign lesions were more common in seventh decade and malignant lesions in eighth decade (Table 1).

Table 1: age range distribution of prostatic lesions

Age range	Benign prostatic hyperplasia	Prostate adenocarcinoma
40-49	02	00
50-59	15	01
60-69	45	08
70-79	26	18
80-89	04	07
90-99	00	06

Frequency of urination was most common presenting symptom (42 cases - 30%) followed by difficulty in voiding (38 cases – 27.14%). (Fig. 1)

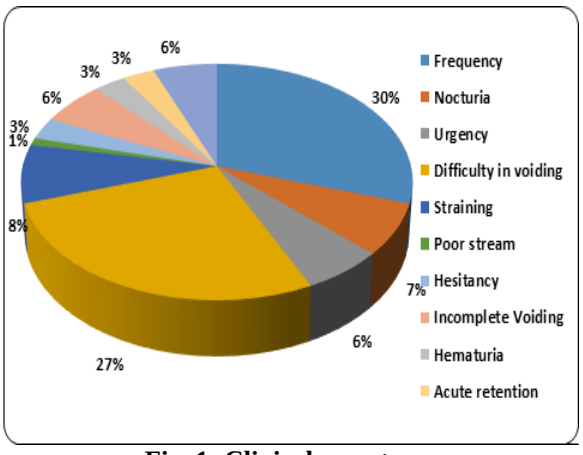

Fig. 1: Clinical symptoms

The commonest histopathological diagnosis was benign prostatic hyperplasia - 90 cases (64.28%), followed by adenocarcinoma-38 cases (27.14%). 5 cases were of chronic prostatitis, 2 cases were of retention cyst, 3 cases were of high grade prostatic intraepithelial neoplasm and 2 cases were of adenosquamous carcinoma (Fig. 2).

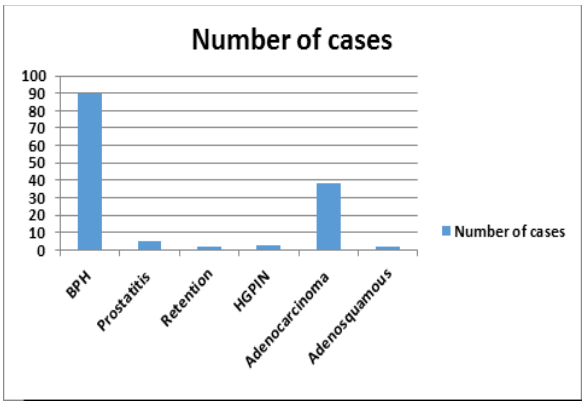

Fig. 2: Histomorphological spectrum of prostate biopsies

HGPIN: High grade prostatic intraepithelial neoplasm, BPH: Benign prostatic hyperplasia.

From 90 cases of benign prostatic hyperplasia, 26 cases (28.88%) had associated chronic prostatitis. The commonest Gleason system score in prostatic adenocarcinoma cases was score 7 (21 cases), followed by score 8 (9 cases), score 9 (5 cases) and score 6 (5 cases), having 52.5%, 22.5%, 12.5% and 12.5% respectively. (Table 2)

Table 2: Gleason system score and number of adenocarcinoma cases

Gleason score	Number of cases	Total cases (%)
6(3+3)	5	5(12.5%)
7(3+4)	10	21(52.5%)
7(4+3)	11	
8(4+4)	7	9(22.5%)
8(3+5)	2	
9(4+5)	2	5(12.5%)
9(5+4)	3	
10(5+5)	0	
Total	40	40(100%)

Adenosquamous carcinoma had score 7 (4+3). Pattern 4 was the most common predominant pattern (21 cases – 52.5%) followed by pattern 3 (14 cases - 35%) and pattern 5 (5 cases – 12.5%). Pattern 1 and 2 were not detected in biopsies. Perineural invasion was seen in 10 (25%) cases out of 40 prostate carcinoma cases; among these 4 cases had Gleason score 7 and 6 cases had Gleason score 8.

Benign prostatic hyperplasia cases had mean prostate specific antigen value of 5.05 ± 3.15 ng per ml with normal level (<4 ng/ml) found in 56 (62.22%) cases; mild elevation (4-10 ng/ml) was seen in 19 (21.11%) cases; modest elevation (10.1-20 ng per ml) was seen in 10 (11.11%) cases; marked elevation of prostate specific antigen (>20 ng per ml) was seen in 5 (5.55%) benign prostatic hyperplasia cases. Prostate carcinoma cases had mean prostate specific antigen level of 59.65 ±38.65 ng per ml with mildly elevated level in four (10.52%) cases; modest elevated level in four (10.52%) cases and marked elevated level in thirty (78.94%) cases; out of these 30 cases, 18 cases were having prostate specific antigen level of even more than 80 ng per ml. Prostatitis cases had mean prostate specific antigen value of 32 ±38.6 ng per ml and HGPIN cases showed mean prostate specific antigen value of 14.8 ±7.8 (Table 3 and Table 4).

Table 3: Mean prostate specific antigen value and histopathological diagnosis

Histopathological diagnosis	PSA level (mean±SD)
Benign prostatic hyperplasia	5.05 ±3.15
Prostatic adenocarcinoma	59.65 ±38.65
High grade prostatic intraepithelial neoplasia	14.8 ±7.8
Chronic prostatitis	32 ±38.6

Table 4: Prostate specific antigen (PSA) value range and prostatic lesions

PSA (ng/ml)	BPH (%)	Prostatitis (%)	Retention cyst (%)	HGPIN (%)	Adenocarcinoma (%)	Adenosquamous carcinoma (%)
<4	56(62.22%)		2(100%)			2(100%)
4-10	19(21.11%)	2(40%)		1(33.33%)	4(10.52%)	
10.1-20	10(11.11%)	1(20%)			4(10.52%)	
>20	5(5.55%)	2(40%)		2(66.66%)	30(78.94%)	
Total	90(100%)	5(100%)	2(100%)	3(100%)	38(100%)	2(100%)

HGPIN: High grade prostatic intraepithelial neoplasm, BPH: Benign prostatic hyperplasia

Discussion

Benign prostatic hyperplasia and prostatic adenocarcinoma are the two of the commonest problems in geriatric men age group and also a concern for urine outflow obstruction. Final diagnosis is made by combination and correlation of digital rectal examination, increased level of prostate specific antigen, and histopatholgical examination of needle biopsy/trucut biopsy.[17] In our study mean age of all cases was 65.5 years, mean age for benign prostatic hyperplasia was 66.07 and mean age for prostatic carcinoma was 72 years. Most common age group overall and for benign lesions was 60-69 years and for malignant lesions it was 70-79 years. All the prostate lesion cases were more than 40 years age group. These findings are compared with Jasani et al., Anushree et al., Aslam et al., and Akhtar et al. and all have almost similar results.[18-21] Most common clinical symptom was frequency of micturition, second is difficulty in voiding secondary to urethral obstruction by enlarged prostatic gland similar to findings by Akhtar et al.[21]

As compared with above all studies, our study shows benign prostatic hyperplasia as the commonest biopsy diagnosis followed by prostate adenocarcinoma. 28.88% cases of benign prostatic hyperplasia was having chronic prostatitis also as comparable to Josephine et al (25.31%).[10]

There is a very well documented and clinical evidence of Gleason system of scoring with serum prostate specific antigen level, prognosis, effectiveness of treatment, tumor aggression and volume of tumor.[10] Commonest Gleason score was 7 in our study, and most predominant was pattern was 4 and then 5 and 3. Deshmukh et al., Shirish et al., and Josephine et al. all have similar results.[22,23,10] Kansal et al study had 62.71% patients in Gleason score 5-7, 13.55% patients with Gleason score 8-10 and 23.72% patients with Gleason score 2-4.[24] Josephine et al., study had 60% patients in Gleason score 5-7, 20.5% patients with Gleason score 8-10 and 15% patients with Gleason score 2-4.[10] Our study had 62.1% patients with Gleason score 5-7 and 37.9% patients with Gleason score 8-10. No cases were of 2-4 Gleason score in our study. This may be due to having more needle biopsy as compared to prostatectomy. 9 cases had perineural invasion (22.5%), out of these 3 had Gleason score of 7 and 6 had Gleason score 8. This is comparable with Kansal et al.[24] in which 4 out of 6 cases with perineural invasion had Gleason score of 8 and more.

Prostate specific antigen is a good tumor marker for monitoring the course of adenocarcinoma and also for early diagnosis. It should not be used alone for diagnosis of adenocarcinoma because it has less predictive value and it is also elevated in benign hyperplastic conditions.[25]

Benign prostatic hyperplasia cases had mean prostate specific antigen value of 5.05 ± 3.15 ng per ml with normal level (<4 ng/ml) found in 56 (62.22%) cases; mild elevation (4-10 ng/ml) was seen in 19 (21.11%) cases; modest elevation (10.1-20 ng per ml)

was seen in 10 (11.11%) cases; marked elevation of prostate specific antigen (>20 ng per ml) was seen in 5 (5.55%) benign prostatic hyperplasia cases. Jasani et al.[18] also had the comparable results with mean prostate specific antigen value of 4.86 ± 3.03; 63.72% with normal prostate specific antigen value, 27.45 with modest elevation and 8.8% with marked elevation. Chronic prostatitis could be the cause for elevation of prostate specific antigen. Prostate carcinoma cases had mean prostate specific antigen level of 59.65 ±38.65 ng per ml with mildly elevated level in four (10.52%) cases; modest elevated level in four (10.52%) cases and marked elevated level in thirty (78.94%) cases; out of these 30 cases, 18 cases were having prostate specific antigen level of even more than 80 ng per ml. Normal prostate specific antigen level was there in one case of adenocarcinoma and also three cases of benign prostatic hyperplasia had PSA value of more than 100 ng per ml. therefore PSA alone cannot be the predictor of malignancy. As the prostate specific antigen value increases, numbers of adenocarcinoma cases raises compared to benign prostatic hyperplasia cases. (Fig. 3)

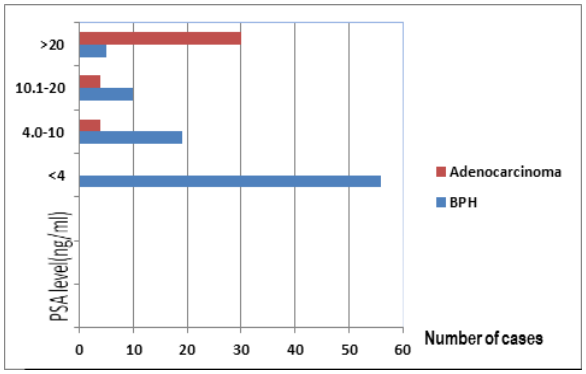

Fig. 3: PSA level compared with benign and malignant prostate lesions

Conclusion

Benign prostatic hyperplasia is the commonest prostatic lesion followed by prostatic adenocarcinoma. Marked elevation of prostate specific antigen is associated with prostate carcinoma more than hyperplasia. PSA alone should not be used as a marker of malignancy. Adenocarcinoma patients have higher age group affected as compared to BPH patients. Frequency of micturition and difficulty in voiding are the commonest presenting features of prostatic lesion patient. Prostate specific antigen value should be measured periodically in elderly men as a screening tool. Each higher value must be followed by histopathological evaluation of prostate biopsy for exact nature of disease confirmation.

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