Clinicopathological study of neoplastic and non-neoplastic lesions of prostate- two years study

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Abstract

Introduction: Among the cancer related deaths in men, prostatic cancer is the second most common to lung cancer. Important cause for prostatic morbidity and mortality includes inflammation, benign nodular enlargement and tumors. Histopathological diagnosis and grading plays a definitive role in the management of prostatic cancer. The current study aims at analyzing clinicopathological features of various neoplastic and non-neoplastic lesions of the prostate.

Materials and Method: The present study included 158 prostatic specimens, which comprises of 157 TURP chips, and 1 prostatectomy specimen. The results were grouped into non-neoplastic and neoplastic lesions. The cases of prostatic adenocarcinoma were graded using Gleason microscopic grading.

Results: Out of 158 prostatic specimens studied; 145 were benign lesions, 4 were premalignant and 9 were malignant lesions. Among benign lesions nodular hyperplasia without prostatitis was the most common. The cancer detection rate with prostatic volume < 40 ml was higher than with >40 ml. Most malignant prostatic lesions showed marked elevation in serum PSA levels (>20 ng/ml). Among the malignant lesions, commonest lesion was prostatic adenocarcinoma.

Discussion: Since low-grade lesions are usually asymptomatic, awareness of serum PSA level estimation, digital rectal examination should be done among elderly males who are prone for malignancy. Male individuals with a positive family history for prostatic carcinoma must undergo relevant screening test.

Keywords: Prostate, Hyperplasia, Adenocarcinoma, PSA, Gleason score

Introduction

The prostate gland is the largest accessory reproductive organ in male. The prostate is an exocrine gland and forms prostatic secretion which is a significant component of seminal fluid.(1) Prostatism and geriatric population go hand in hand. Being hormone (androgen) dependent, an array of lesions comprising of both benign as well as malignant lesions are seen affecting this population.(2)

Important cause for prostatic morbidity and mortality includes inflammation, benign nodular enlargement and tumors. Benign prostatic hyperplasia (BPH) alone affects 210 million males worldwide, and it is so common in advanced ages that it can be considered as a part of normal ageing process. BPH is the most common urologic disorder in men beyond 40 years of age group and is almost always present in men aged 80-90 years of age group.(3) Furthermore, prostatic tumors are a very important cause of male morbidity and mortality and prostate cancer is second only to lung cancer among cancer- related deaths in men. Prostate cancer is responsible for 3% of all deaths in men above 55 years of age.(3)

A combination of digital rectal examination, transrectal ultrasonogram and needle biopsy can prove to be a powerful diagnostic tool in the routine diagnosis of benign and malignant prostatic lesions.(2) A relatively new development in the prostatic histopathology is the identification of premalignant conditions that can help in early diagnosis of prostate cancer.(4) The premalignant lesions of prostate include prostatic intraepithelial neoplasia (PIN) and atypical adenomatous hyperplasia (AAH) and recently, the new lesion added to the list of premalignant lesion is proliferative inflammatory atrophy (PIA).(5)

Histopathological diagnosis and grading plays a definitive role in the management of prostatic cancer.(6) The current study aims at analyzing clinicopathological features of various neoplastic and non-neoplastic lesions of the prostate in the randomized study for a period of two years.

Materials and Method

This is a cross sectional observational study carried out in tertiary care hospital, at Govt. medical college and hospital, Latur (Maharashtra, India) prospectively during the duration January 2015 to December 2016. The specimens from patients diagnosed and operated in the same institute were included and specimen sent without complete information and non-prostatic tissues were excluded. The prostatic material included prostatic biopsies, transurethral resection of prostate (TURP) chips and prostatectomy specimen.

Our study included 158 prostatic specimens, which comprises of 157 TURP chips, and 1 prostatectomy specimen. No radical prostatectomy specimens were received.

In cases of TURP chips 3 to 4 cassettes were prepared in each case, which accommodated approximately 50% of total tissue, and weighed

approximately 9 to 12gms. Specimens weighing ≤12 grams were submitted entirely. In general, random chips were submitted; however, if some chips were firmer or had a yellow or orange-yellow appearance, they were preferentially submitted.

In case of prostatectomy specimens, multiple sections were made thickness of 3 to 5 mm. The slice in which tumor appears closest to the resection margin, was submitted entirely after dividing into adequate number of sections.

All the tissues were fixed in 10% formalin and paraffin processed. 3 to 5 micron sections were cut and stained with routine Hematoxylin and Eosin (HE) stain.

All the lesions were grouped into non-neoplastic and neoplastic lesions. The cases of prostatic adenocarcinoma were graded using Gleason grading. The clinical and histological data so obtained were analyzed and compared with other similar studies.

Statistical analysis: All data were statistically analyzed by using Chi-square test. Microsoft word and Excel have been used to generate graphs, tables, pie diagrams etc.

Results

Of the 158 cases, 145 (91.77%) cases were benign, 4 (2.53%) cases were premalignant and 9 (5.7%) cases were malignant. Benign prostatic hyperplasia was the most common encountered histopathological diagnosis seen in 141 (89.24%) cases (Table 1). In the present study, chronic non-specific prostatitis formed the majority among the inflammatory lesions and 3 cases of non-specific granulomatous prostatitis were identified. Foci of chronic prostatitis were seen in majority of cases of BPH. In the present study 4 premalignant lesions were identified, 2 (1.26%) cases were low grade PIN, 1 (0.63%) was high grade PIN and 1(0.63%) was atypical adenomatous hyperplasia (AAH). Two patterns of PIN were seen in the present study - papillary pattern where the epithelium was thrown in to papillary projections and cribriform pattern showing glands with epithelium forming a cribriform pattern were identified. All malignant cases were adenocarcinoma of prostate.

Table 1: Final histopathological diagnosis in the cases studied

Final diagnosis	No. of cases	Percentage
Benign prostatic hyperplasia With prostatitis 62 (43.9%) Without prostatitis 79 (56.1%)	141	89.24
Stromal nodule	01	0.63
Low grade PIN	02	1.26
High grade PIN	01	0.63
Granulomatous prostatitis	03	1.9
Atypical adenomatous hyperplasia	01	0.63
Adenocarcinoma	09	5.7
Total	158	100

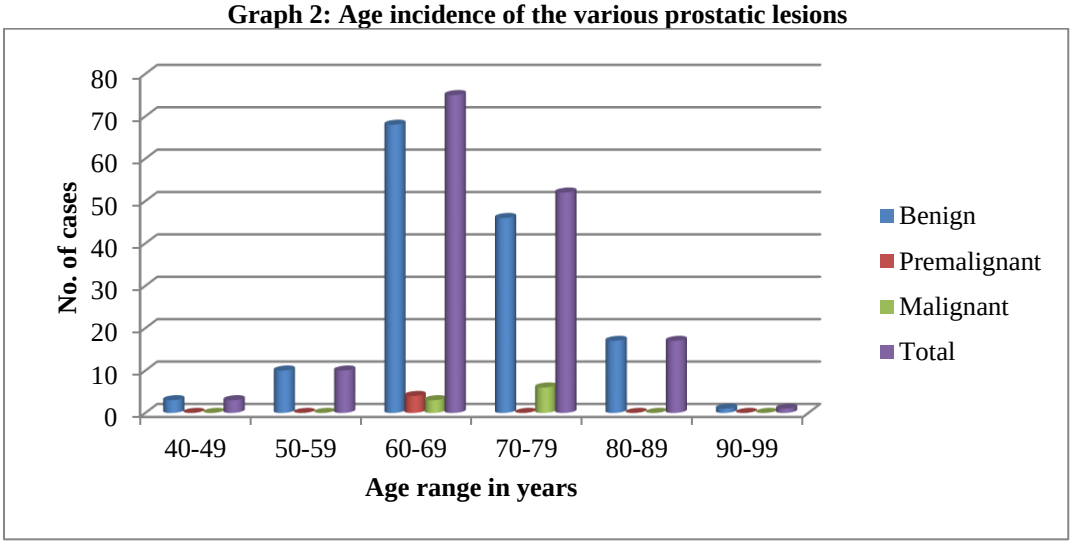
Mean age of patients with prostatic pathology was 69 years. Maximum benign cases i.e. 68 (46.9%) were seen in the age group 60-69 years. Youngest benign case was 45 years old and oldest was 90 years. Peak occurrence of malignant cases was distributed in two age groups, i.e. in 60-69 and 70-79 years. Youngest patient with malignancy was 60 years and oldest patient was 72 years (Table 2).

Table 2: Age incidence of the various prostatic lesions

Age (years)	Benign N (%)	Premalignant N (%)	Malignant N (%)	Total N (%)
40-49	3 (2.06)	-	-	3 (1.9)
50-59	10 (6.89)	-	-	10 (6.32)
60-69	68 (46.89)	4 (100)	3 (33.33)	75 (47.5)
70-79	46 (31.72)	-	6 (66.66)	52 (32.9)
80-89	17 (11.72)	-	-	17 (10.8)
90-99	1 (0.68)	-	-	1 (0.63)
Total	145 (100)	4 (100)	9 (100)	158 (100)

Chi Square test: 9.98; df: 10 P>0.05 NS (not significant)

Graph 2: Age incidence of the various prostatic lesions



In the present study, clinically digital rectal examination findings showed firm nodularity in 148 (93.67%) cases and presence of hard nodule in 10 (6.32%) cases. Out of 148 lesions which showed firm nodularity, all cases were benign. Among the 10 cases that showed hard nodule on DRE, 1 case was found to be granulomatous prostatitis and 9 cases were malignant on histopathological examination.

Frequency was the most common symptom in benign lesions in 97 (67%) cases followed by acute retention in 90 (62%), hesitancy in 24 (16%) and difficulty in voiding in 18 (12%) cases. In malignant lesions, common symptoms were dysuria in 8 (88.9%) cases, incomplete voiding in 5 (55%) and difficulty in voiding in 5 (55%) cases. However, when both the lesions were compared poor stream was positively associated with benign lesions and incomplete voiding, dysuria and hematuria were significantly associated ($p \leq 0.05$) with malignant lesions. Premalignant lesions had same clinical symptoms as seen in benign lesions as they were mostly associated with benign lesions.

In the present study, volume of various prostatic lesions on ultrasonogram (USG) was assessed. Various prostatic lesions had prostatic volume ranging from 31-130 ml. Out of 145 benign lesions, 63 (43.44%) had prostatic volume more than 80 ml and 25 (17.2%) had volume ranging from 61-70 ml. Among all inflammatory lesions associated with BPH, 38 (58.46%) cases had prostatic volume more than 80 ml. All premalignant lesions had prostatic volume ranging from 31-80 ml. Volume of 3 (33.33%) cases of adenocarcinoma had more than 80 ml, while 6 (66.66%) cases had volume ranging from 31-80 ml. Lowest volume 31 ml and highest volume 130 ml were noted. Prostatic volume of various prostatic lesions was not significantly associated with P value > 0.05.

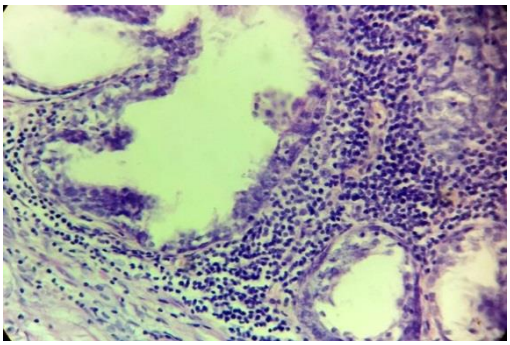
In our study, serum PSA was done in all cases. 35 (53.03%) cases out of 66 cases of inflammation had mild elevation of serum PSA levels in the range of 4.1-10 ng/ml. A total of 79 (54.5%) benign cases had serum PSA levels in the range of 0-4 ng/ml. 61 (42.06%) cases had modest elevation in serum PSA in the range of 4.1-10 ng/ml and 3 (2.06%) cases had serum PSA in the range of 10.1-20 ng/ml. Five (55.55%) out of 9 malignant cases had severely elevated serum PSA levels >20 ng/ml. When serum PSA levels in benign and malignant lesions were compared, serum PSA in the range of 0-4 ng/ml was significantly associated with benign lesions (P value < 0.007) and serum PSA > 20 ng/ml was significantly associated with malignant lesions (P value < 0.01).

Clinically on the basis of presenting complaints, digital rectal examinations and serum PSA levels, 148 (93.7%) cases were diagnosed as benign lesions while 10 (6.3%) cases were of prostatic carcinoma. But after histopathological examinations 145 cases were found benign, 4 cases were premalignant and 9 cases were malignant.

In present study, on microscopy adenofibromyomatous hyperplasia was the most common variant seen in 146 cases (Table 3) (Fig. 1).

Table 3: Microscopic findings in benign lesions

Microscopy	No. of cases
Adenofibromyomatous type	146
Inflammation Chronic 60 Acute on chronic 02 Granulomatous 03	65
Squamous metaplasia	03
Adenomatous hyperplasia	02
Basal cell hyperplasia	01
Fibromyomatous type	01



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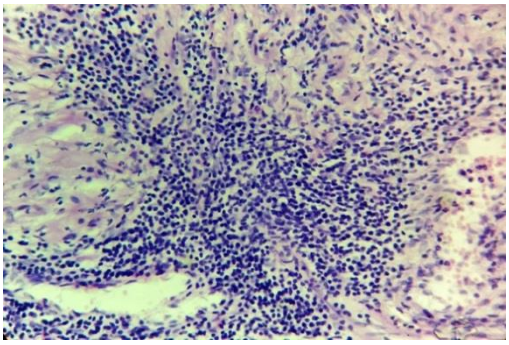

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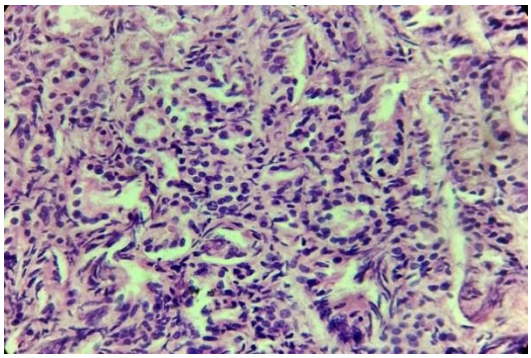
Fig. 1 (A&B): Chronic prostatitis shows periglandular and stromal infiltration of lymphocytes, histiocytes and plasma cells. (H&E, 40x)

Table 4: Microscopic findings in malignant lesions

Microscopic findings	No. of cases N (%)
Acinar pattern	7 (77.77)
Cords	4 (44.44)
Nests	4 (44.44)
Sheets	3 (33.33)
Cribriform	1 (11.11)
Trabeculae	-

The commonest pattern in cases of adenocarcinoma was the acinar pattern in 7 cases (77.77%) (Table 4) (Fig. 2).



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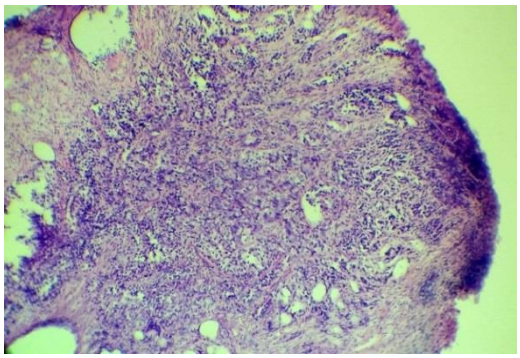

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Fig. 2: (A&B) Prostatic adenocarcinoma, Gleason's pattern (3+4): Predominantly well-formed glands with a lesser component of poorly-formed/fused/cribriform glands (H&E, 40x)

Table 5: Incidence of Carcinoma with reference to Gleason's Score (maximum score 10)

Gleason's Score	No. of cases (%)	Differentiation of tumor (GS)
2	-	Well differentiation (2-4)
3	-	
4	2 (22.22)	
5	-	Moderate differentiation (5-7)
6	-	
7	4 (44.44)	
8	-	Poor differentiation (8-10)
9	1 (11.11)	
10	2 (22.22)	
Total	9 (100)	

Gleason grading of the 9 cases of adenocarcinomas showed that moderately differentiated carcinomas (GS 5-7) comprised the largest group with 4 cases (44.4%) and poorly differentiated carcinomas (GS 8-10) was the next most frequently with 3 cases (33.3%); well differentiated cancers with Gleason score of 2-4 comprised 2 cases (22.2%).

Discussion

The study focuses on clinicopathological spectrum of non-neoplastic and neoplastic lesions of prostate followed by assessment and comparisons of prostatic volume with histopathological findings.

The incidence of prostate pathologies more specifically BPH and adenocarcinoma is increasing in

India owing to westernization in culture. Nowadays, various modalities of treatment include hormonal therapy, surgical excision in the form of TURP or prostatectomies have gained more weightage. In our study, prostatic chips from TURP procedure comprised the majority of samples received i.e. 157 (99.36%) and 1 (0.63%) was prostatectomy specimen. According to the literature Chandanwale et al[1] and Khatib et al,[2] TURP is the most commonly performed procedure whereas prostatectomy is least commonly observed procedure in India.

In our study, mean age of patients with prostatic pathology was 69 years. Our results were comparable to the studies done by Anushree et al[7] and Deshmukh et al.[8]

In the present study, frequency (67%) was the most common symptom in benign lesions and malignant lesions had common symptoms dysuria (88.9%), incomplete voiding (55%) and difficulty in voiding (55%). However, when both the lesions were compared poor stream was positively associated with benign lesions and incomplete voiding, dysuria and hematuria were significantly associated with malignant lesions. Anushree et al[7] found frequency to be the most common symptom accounting for 36.67% followed by difficulty in voiding (28%) and acute retention (22%). Puttaswamy et al[9] study showed the most common symptom in the 62 cases studied was hesitancy (51.6%) and frequency (50%) followed by dysuria (41.9%) and acute retention (38.7%). In the malignant cases, Anushree et al[7] found frequency (38.5%), incomplete voiding (38.5%), and dysuria (38.5%) as the most common symptoms.

In the present study volume of various prostatic lesions on USG was assessed. Various prostatic lesions had prostatic volume ranging from 31-130 ml. Out of 145 benign lesions, 63 (43.44%) had prostatic volume more than 80 ml, while 6 (66.66%) cases had volume ranging from 31-80 ml. Yoon et al[10] studied 474 cases based on TRUS guided biopsy. In patients with prostate volume >40 ml, the cancer detection rate was 19% and that with <40 ml was 33.2%. In present study the cancer detection rate with prostate volume >40 ml was 4.9% and that with <40 ml was 12.5%. No other studies have been found for the comparison of occurrence of benign and inflammatory lesions with the prostatic volumes, so further studies will be required to arrive at conclusions. Uzzo et al[11] reviewed 1021 TRUS guided prostate biopsies to determine if cancer detection varied based on prostate size. Small prostate were noted in 675 cases of which 38% had cancer detected and 346 patients with large prostate had 23% cancer detected and concluded that cancer detection rate in patients with small prostate was higher than larger prostate. This was comparable to present study.

In our study, 79 (54.5%) benign cases had serum PSA in the range of 0-4 ng/ml and 5 malignant cases had severely elevated serum PSA levels >10 ng/ml. Our results were consistent with the results of the studies done by Anushree et al,[7] Chandanwale et al[1] and Akhter et al.[12]

Most patients over the age of 50 years will have histological evidence of BPH and many will suffer symptoms from urethral compression. Data indicate that on microscopic examination both epithelium and stroma are involved in varying degrees and predominant pattern is fibroadenomatous hyperplasia. Mittal et al,[13] Bal et al[14] and Deshmukh et al[8] in their studies, also observed similar findings of 93%, 87% and 92.04% respectively.

In the present study adenofibromyomatous hyperplasia was seen in 146 cases where hyperplasia of both epithelial and stromal components was seen. The findings of present study were comparable to Anushree et al,[7] Deshmukh et al[8] and Franks[15] studies where the most common histological pattern of BPH was found to be adenofibromyomatous type followed by fibroadenomatous.

A total of 65 (41.13%) cases of all the prostatic lesions showed prominent inflammation both acute on chronic and chronic type. Chronic inflammation was seen in 60 cases among all inflammatory lesions. Foci of chronic inflammation were seen in majority of cases of BPH (Fig. 1). Mittal et al[13] studied 185 consecutive prostatic specimens and found 57.83% showing inflammation. In cases of chronic non-specific prostatitis, lymphocytes, plasma cells and macrophages were seen in the stroma and lumen of the ducts showed secretions and neutrophils. In our study, occurrence of prostatic inflammation was relatively higher than Abdel-Meguid et al[16] and Wadgaonkar et al[17] studies where it was 20.1% and 23.75% respectively.

All the cases of prostatic carcinoma were prostatic adenocarcinoma. A total of 9 (5.7%) cases of prostatic carcinoma were identified in our study. This was comparable to the Deshmukh et al,[8] Mittal et al[13] and Kumar et al[18] studies with incidences 7.96%, 7.02% and 4.3% respectively, while the results of Obiorah[19] studies where 37.4% was much higher than the present study. This might be due to less sample size and geographic variation.

The commonest pattern in case of adenocarcinoma we found was the acinar pattern in 7 cases (77.77%), cords in 4 cases (44.44%), nests in 4 cases (44.44%), sheets in 3 (33.33%) cases, and cribriform in 1 case (11.11%). This was comparable to Mittal et al[13] study which showed small acinar carcinoma pattern to be the most frequent (53.8%) followed by solid and trabecular pattern (38.46%) and the Obiorah et al[19] study showed majority (53.5%) of the adenocarcinomas were histologically of the large acinar variety, followed by small acinar pattern, which occurred in 17.68%. Solid/Trabeculae and cribriform patterns occurred in 15.7% and 13.1%, respectively (Table 6).

Table 6: Comparison of microscopic findings in malignant lesions

Authors	Microscopic findings (Percentage)				
	Acinar	Cords	Nests	Solid sheets	Cribriform
Mittal et al[13]	53.8	-	-	38.46	-
Obiorah et al[19]	71.18	-	-	17.68	13.1
Present study	77.77	44.44	44.44	33.33	11.11

In the present study Gleason grading of the 9 cases of adenocarcinomas showed that moderately differentiated carcinomas (GS 5-7) comprised the largest group with 4 cases (44.4%). This was consistent with the studies done by Chandanwale et al(1) and Anushree et al.(7)

Conclusions

In conclusion, most of the cases of prostatic adenocarcinoma encountered were of high grade. Since low-grade lesions are usually asymptomatic, awareness of serum PSA level estimation, digital rectal examination should be done among elderly males who are prone for malignancy. Male individuals with a positive family history for prostatic carcinoma must undergo relevant screening test. The correct diagnosis of mimickers of adenocarcinoma should be made in order to prevent radical prostatectomy, which has high rate of morbidity in elderly males. Since serum PSA was increased in few benign and most of the malignant cases, newer modalities of measuring PSA like PSA density, PSA velocity, age specific reference rates should be adopted to distinguish between benign and malignant lesions.

Limitations of study

1. This was tertiary care hospital based study.
2. Due to lack of facilities of Immunohistochemistry, it was not done in all the suspected cases.
3. In the cases of prostatic chips by TURP the tissue obtained was from the transition zone and not from the peripheral zone, hence diagnosis of malignancy may be missed in spite of strong clinical suspicion of malignancy.

Clinical implications

The correct diagnosis of mimickers of adenocarcinoma should be made in order to prevent radical prostatectomy, which has high rate of morbidity in elderly males. Since serum PSA was increased in few benign and most of the malignant cases, newer modalities of measuring PSA like PSA density, PSA velocity, age specific reference rates should be adopted to distinguish between benign and malignant lesions. Diagnosis of HGPIN should be included since it is a precursor of adenocarcinoma. Most of the cases of prostatic adenocarcinoma encountered were of high grade. Since low-grade lesions are usually asymptomatic, awareness of serum PSA level estimation, digital rectal examination should be done among elderly males who are prone for malignancy. Male individuals with a positive family history for prostatic carcinoma must undergo relevant screening test.

Conflict of Interest: None to declare

Source of funding: Nil

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