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Original Research Article

Histopathological Spectrum of Lesions of Prostate

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Abstract

Prostatic lesions like Benign Prostatic hyperplasia (BPH), prostatitis, and adenocarcinoma account for significant mortality and morbidity in the geriatric male population. Prostate specific antigen (PSA) level has become the most popular screening method for the detection of different prostatic lesions. We aim to study the Histopathological spectrum of the lesions of the prostate and its correlation with PSA. A Cross-sectional study was done on 75 prostatic specimens. Relevant clinical data, PSA levels, and histopathological diagnosis were noted. The histopathological spectrum of different prostatic lesions was categorized into benign and malignant lesions. PSA correlation was done. Sensitivity and specificity were calculated at PSA cut-off levels of 4ng/ml, 10ng/ml, and 20ng/ml. 85.3% (n=64) of the lesions were benign while 14.7% (n=11) of the lesions were malignant. BPH with chronic prostatitis was the most common benign lesion accounting for 45.3% cases (n=34). All the malignancies were adenocarcinoma and were mostly of Gleason's Grade 2. PSA showed maximum sensitivity i.e. 100% at level 4ng/ml but showed minimum specificity of 43.30% and specificity was seen increasing with increasing PSA cut off and was maximum at level 30ng/ml i.e.95.08%. The most frequently encountered lesion of the prostate is BPH with chronic prostatitis. PSA is an early and sensitive marker but has a limitation at a cut-off value of 4ng/ml; but it lacks specificity.

Keywords: Prostate, Prostate specific antigen (PSA), Histopathological spectrum, Benign prostatic hyperplasia (BPH), Prostatitis, Adenocarcinoma of prostate, Gleason grade.

INTRODUCTION

The Prostate is one of the most commonly affected organs in males with increasing age, accounting for significant mortality and morbidity. Lesions of the prostate display a parallel increase in incidence with increasing age. Globally prostate cancer is the second most frequently diagnosed cancer (Daniyal *et al*., 2014) and the fifth leading cause of death in men (Ferlay *et al*., 2010). In India, there is an increasing trend in the incidence of prostatic cancer, with the increasing life expectancy of the male population.

The most common lesion of the prostate is Benign Prostatic Hyperplasia (BPH) (Aslam *et al*., 2013). It is the non-malignant adenomatous overgrowth of the prostate gland. It presents with lower urinary tract symptoms; urine obstruction being the most common due to location of the urethra concerning the prostate. Other symptoms of prostatic lesions include-increased frequency in micturition, presence of blood in semen or urine, and chronic pelvic pain. Adenocarcinoma of the prostate is a malignant condition of the prostate which is commonly screened for in the population by testing the PSA levels of men. It is the most commonly used serum marker for cancer. High serum PSA levels are indicative of prostate carcinoma but it lacks specificity and sensitivity.

The characteristics of the prostatic lesions are extensively studied abroad. We decided to do this study as part of our Indian council of medical research Short term student project because prostate was one of the common specimen received in our department of Pathology. Our objectives were 1. To study the spectrum of histopathological features of lesions of prostate, 2. To find out the incidence of prostate pathologies according to age and 3. To study PSA levels in different prostatic lesions.

MATERIAL AND METHOD

The present descriptive cross-sectional study was carried out in the Department of Pathology at Dr. D. Y. Patil Medical College, Hospital and Research

Centre, Dr. D. Y. Patil Vidyapeeth, Pimpri, Pune-411018. Institute Ethics Committee Clearance (IECC) IESC/FP/2020/45 was obtained before the start of the study. Retrospective data was collected over two months from the medical records of the department. Data of 75 specimens were collected, which included prostate biopsy, TURP, and prostatectomy specimens. The specimens of patients less than the age of 40 years and inadequate biopsies for histopathological reporting were excluded.

The specimens were fixed routinely in 10% formalin, embedded with paraffin, and cut with microtome at 4 microns. The sections were further stained with haematoxylin and eosin stains. Sections were examined under light microscopy and a histopathological diagnosis was made according to the HPE features. BPH specimens showed hyperplastic prostatic glands lined by 2 layers of cells - columnar epithelial cells and a peripheral layer of flattened basal cells and the hyperplastic nodules composed of variable proportions of proliferating glandular elements and fibromuscular stroma. Prostatitis was an inflammatory lesion further divided into acute and chronic. Acute prostatitis was characterized by neutrophilic infiltration while chronic prostatitis presented with lymphocytic infiltration. Basal cell hyperplasia was characterized by a basophilic appearance of cells having a scanty cytoplasm and blue nuclei. Prostatic intraepithelial neoplasia (PIN); a premalignant lesion of the prostate was characterised by medium to large ducts and acini with enlarged hyperchromatic nuclei and amphophilic cytoplasm. Adenocarcinoma of prostate was characterised by glands that were lined by a single uniform layer of cuboidal or low columnar epithelium, lacking the basal cell layer. The glands were smaller than that seen in benign lesion and were crowded together and characteristically lack branching and papillary infolding. The cytoplasm of the tumour cells ranged from pale-clear (as in benign glands) to a distinctive amphophilic (dark purple) appearance. Nuclei were enlarged and often contained one or more prominent nucleoli. The adenocarcinoma cases were graded according to Gleason's grade (Epstein *et al*. 2016) which is based on 2 features- Degree of glandular differentiation and distribution and growth pattern of the tumour in relation to the stroma.

Gleason's grade was as follows:

1 = Gleason score 3+3=6
2 = Gleason score 3+4=7
3 = Gleason score 4+3=7
4 = Gleason score 8 (4+4=8, 3+5=8, 5+3=8)
5 = Gleason score ≥ 9 (4+5=9, 5+4=9, 5+5=10)

The PSA levels were obtained from the central clinical laboratory. The device used for the calculation of serum PSA was Architect plus. Serum PSA was estimated using. Chemiluminescent Micro-Particle Immunoassay which was a two-step method and estimated PSA by sandwich assay utilizing Anti-PSA coated paramagnetic microparticles.

The data collected were tabulated and statistically analyzed by calculating the P-value for the age and specificity and sensitivity of the PSA levels at different cut off were calculated by using the formula.

Sensitivity = TP/ TP+FN
(TP=true positive, FN=false negative)
Specificity =TN/ TN+FP
(TN=true negative, FP= false positive)

RESULTS

We studied 75 prostatic biopsy samples for histopathological evaluation. Maximum lesions occurred in the 8th decade of life, the incidence being 40%(n=30). The p-value calculated correlating the incidence of benign and malignant lesions with age was 0.97 hence it was statistically not significant. Histopathological diagnosis revealed, 85.3% (n=64) benign lesions while only 14.7%(n=11) of the lesions were malignant. The most common diagnosed lesion was BPH (with and without inflammation) accounting for 80%(n=60) cases. BPH with inflammation was the most common associated lesion of BPH with 45.3%(n=33) cases. Other associated lesions of BPH included basal cell hyperplasia and chronic non-granulomatous prostatitis. The histopathological spectrum of the prostatic lesion was as shown in Table 1.

Table-1: Histopathological spectrum of the prostatic lesions in Study group

HPE Diagnosis	No. of cases	Percentage
BPH	26	34.70
BPH with prostatitis	33	44.00
BPH with non- specific granulomatous prostatitis	1	1.30
Basal cell hyperplasia	1	1.30
Prostatic intraepithelial neoplasia	3	4.00
Prostatic Adenocarcinoma	11	14.70
Total	75	100

BPH with prostatitis was the most frequently encountered lesion. Adenocarcinoma of prostate was graded using Gleason's grade pattern. Combined grade was used using primary and secondary scoring pattern. Grade 1 was at score </= 6 Grade 2 at score 7-8 and grade 3 when score is >8. The most common grade seen

in our study was Grade 2, moderately differentiated carcinoma. The various histopathological features of prostatic lesions of the study group were as shown in Figure 1 and 2.

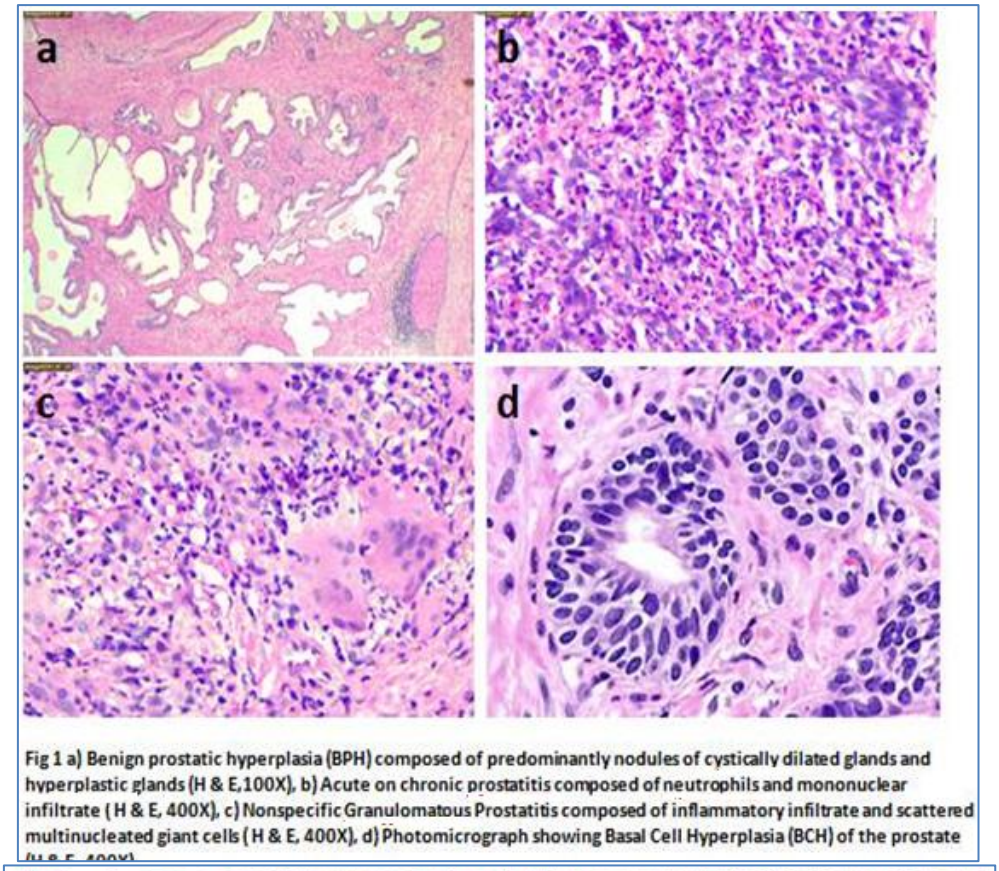

Fig 1 a) Benign prostatic hyperplasia (BPH) composed of predominantly nodules of cystically dilated glands and hyperplastic glands (H & E,100X), b) Acute on chronic prostatitis composed of neutrophils and mononuclear infiltrate (H & E, 400X), c) Nonspecific Granulomatous Prostatitis composed of inflammatory infiltrate and scattered multinucleated giant cells (H & E, 400X), d) Photomicrograph showing Basal Cell Hyperplasia (BCH) of the prostate

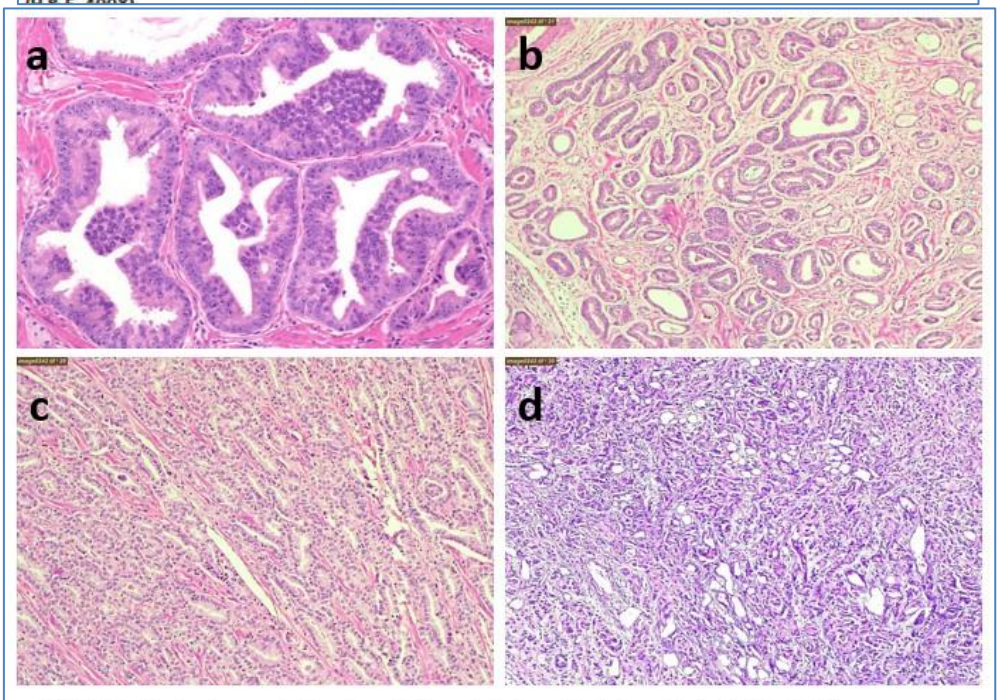

FIGURE 2 : Photomicrograph showing a)High grade intraepithelial neoplasia (H & E, 400X),
b) Adenocarcinoma of prostate, Gleason Grade 1(3+3=6) (H & E, 100X),
c) Adenocarcinoma of prostate, Gleason Grade 2(3+4=7) (H & E, 100X),
d) Adenocarcinoma of prostate, Gleason Grade 4(4+4=8) (H & E, 100X)

The PSA levels of prostatic lesions were as shown in Table 2.

Table-2: PSA level in different Prostatic lesions

PSA LEVELS (ng/dl)	Benign prostatic lesions	Malignant prostatic lesions
>2.5	13	0
2.5-3.9	13	0
4-9.9	19	1
10-19.9	9	5
20-30	4	4
>30	3	4
TOTAL	61	14

It was observed that in a majority of benign lesions - BPH, it was <4ng/dl, BPH with chronic prostatitis had 4-10ng/dl, PIN had >10ng/dl and most of the malignant lesions had PSA value 10-50ng/dl. BPH with chronic prostatitis showed higher PSA levels than that observed in patients suffering from BPH alone.

Sensitivity and specificity of PSA was calculated different cut-offs. The results are shown in Table 3.

Table-3: Sensitivity and specificity of PSA according to different cut-offs

PSA levels (ng/dl)	Sensitivity (%)	Specificity (%)
4	100	43.30
>10	92.86	73.77
>20	57.14	88.52
>30	50	95.08

DISCUSSION

In our study we found a cluster of lesions in the 8th decade of life, this finding was similar to Nwafor *et al*. (Nwafor *et al*., 2015) who found maximum instances in the 71-79 age group. Josephine A. (Josephine., 2014), Forae *et al*. (Forae *et al*., 2011) also found maximum cases occurring in the seventh decade of life.

Maximum lesions were benign, which also was in accordance with the previous studies conducted by Buch A. (Buch *et al*., 2021) who found 80% benign cases and Albasri (Albasri *et al*., 2014) who showed 82.3% prostatic lesions were diagnosed benign. BPH is the most common prostatic lesion. The main androgen stimulant in causing this hypertrophy is DHT (dihydrotestosterone) which is secreted by stromal cells of the prostate. DHT further binds to the androgen receptor to stimulate FGF (fibroblast growth factor) and transforming growth factor (TGF) stimulating stromal and glandular hypertrophy. During puberty due to the action of DHT, the prostate doubles in size. Around the age of 25, it starts to grow again, this growth happens for the rest of life, hence giving rise to BPH in later life.

A maximum number of cases of BPH were associated with chronic prostatitis; similar results were seen in studies conducted by Edlin RS (Edlin *et al*., 2012) *et al*. and Josephine A (Josephine. 2014) who found 61% cases of BPH associated with inflammation.

BPH is commonly found to be associated with prostatitis. This is because the urethra passes through the prostate gland, so when there is hypertrophy of the gland it leads to urinary retention due to obstruction of the urethra. The microbes found in the stagnant urine increase the chances of the development of a chronic infection of the urinary bladder and the prostate.

Besides BPH we also found 1 case of basal cell hyperplasia which is a benign mimicker of prostate carcinoma. Mahapatra *et al*. (Mahapatra *et al*., 2019) who studied various mimickers of prostate carcinoma also found basal cell hyperplasia to be the most common. Other benign lesions that mimic adenocarcinoma are prostate atrophy, clear-cell hyperplasia, cribriform hyperplasia, and very rarely atypical adenomatous hyperplasia. Out of these, we found only single case of basal cell hyperplasia. It is essential to be aware of these mimickers by the pathologist to avoid overdiagnosis of Prostatic carcinoma.

All the adenocarcinomas were graded according to Gleason's grade. In our study, the maximum number of cases was of Gleason's grade 2. The previous studies conducted by Capogrosso *et al*. (Capogrossa *et al*., 2018) show 91% of the cases were of Gleason Grade 1 adenocarcinoma, while Albasri *et al*. (Albasri *et al*., 2012) conducted a study revealed, Gleason's grade 2 was the most frequent. This is because, due to the advent of newer diagnostic techniques, and regular PSA screening, the carcinoma of the prostate is detected at an earlier stage and hence has a better prognosis and survival rate.

We found that most cases had a slightly elevated PSA level, irrespective of whether they were benign or malignant. Our study found that the inflammatory lesions associated with BPH showed higher PSA level than that with BPH alone, This finding was similar to that of Vuvren *et al*. (Van Vuuren *et al*., 2012), who found higher PSA levels in patients with an inflammatory condition associated with the primary prostatic lesion. This can be explained due to the fact that the normal architecture of the prostate is disturbed due to underlying pathology and the cell integrity is lost which leads to the release of PSA into circulation. Serum PSA value increases depending on the extent of underlying pathology. However, as a screening test for prostate cancer, PSA remains controversial as it lacks sensitivity and specificity, PSA levels were raised not only in carcinoma but also in BPH with inflammation and PIN. There was no specific cut off identified for detecting malignancy. We found that the sensitivity reduced and specificity increased with higher cut off of PSA.

Limitation: This was a short term student project of two month duration during COVID -19 Pandemic, hence the sample size is less.

CONCLUSION

The most common pathology in prostatic lesions was benign prostatic hyperplasia. This was very frequently associated with evidence of prostatitis which caused increase in PSA level. The sensitivity and specificity of PSA is variable at different cut off value. This proves that PSA can be used for screening, but histopathology remains the gold standard for definite diagnosis of prostatic lesions.

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