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Histopathological spectrum of prostatic lesions in surgical biopsy specimenswith special reference to hormone receptor status in malignant cases

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ABSTRACT:

Introduction : Diseases of the prostate are common causes of morbidity and mortality in adult males. Benign prostatic hyperplasia is an extremely common disorder in men over the age of 50.Other frequently encountered diseases affecting the prostate are prostatitis and prostatic cancer. Histopathological examination of prostate biopsy specimen is required to rule out the benign or malignant enlargement of prostate gland.Analysis of steroid receptors in the tumor may predict the value of endocrine therapy. High levels of androgen receptor as measured immunohistochemically are associated with aggressive clinic-pathological features.

Aims and Objectives:

1. To study the histological patterns of prostatic lesion in surgical biopsy specimens.
2. To study the expression of androgen receptor, oestrogen receptor and progesterone receptor in prostatic adenocarcinoma, using immunohistochemistry (IHC).

Materials and Methods: A 6 year retrospective cross sectional study was carried out between November 2015 to October 2021 which includes 76 specimens.

Results:A total of 76 specimens were studied out of which 47 (61.84%) were Benign Prostatic Hyperplasia (BPH),making it the commonest lesion. 11 (14.47%) were BPH with non specific prostatitis while 2 (2.63%) were BPH with granulomatous prostatitis. BPH with Prostatic Intraepithelial Neoplasia (PIN) was seen in 4 (5.26%) of the specimens. Only 12 (15.79%)were malignant. All the malignancies were Adenocarcinomas. The mean age of BPH cases was 68.5years ranging from 54 to 80 years. The malignancies were seen in the seventh and the eight decades.The sensitivity of immunohistochemistry with ER, PR &
AR are0%, 41.67% & 100% respectively.

Conclusions:BPH is most accounted lesion the prostate compare to pre-malignant (PIN) and malignant lesions particularly in older age group above 60 years. Screening protocols and awareness programs of prostatic cancer need to be introduced for early detection and treatment. Immunohistochemistry should be done in malignant cases with regard to sex steroid receptor status and also supports the view that anti-androgen and anti-progesterone therapy is helpful in the treatment of prostatic adenocarcinoma.

Keyword: Benign prostatic hyperplasia, Histopathological examination, Prostatic adenocarcinoma, Imunohistochemistry.

I. INTRODUCTION :

The prostate is the largest accessory reproductive organ in male.The prostate is an exocrine gland and forms a significant component of seminal fluid.Diseases of the prostate are common causes of morbidity and mortality in adult males.Benign prostatic hyperplasia (nodular hyperplasia) is an extremely common disorder in men over the age of 50 years.Prostate cancer is the second most common cause of cancer death in men in the most developed countries and its incidence is increasing in developing countries.High grade prostatic intraepithelial neoplasia (PIN) is considered as premalignant condition of of prostatic adenocarcinoma. Age is the most important risk factor of prostatic cancer.It is rare under the age of 40 years and its incidence increases exponentially with age.[1]

Analysis of steroid receptors in the tumor may predict the value of endocrine therapy.[2,3] High levels of androgen receptor as measured immunohistochemically are associated with aggressive clinico pathological features and decreased PSA-survival.[4] In prostatic carcinoma, cells often immune reactive for androgen and progesterone receptors[1,5,6],but much less so for oestrogen receptors, the latter is related to the Gleason's grade and score[7].

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Aims and Objectives:

1. To study the histological patterns of prostatic lesion in surgical biopsy specimens.
2. To study the expression of androgen receptor, oestrogen receptor and progesterone receptor in prostatic adenocarcinoma, using immunohistochemistry (IHC).

II. MATERIALS AND METHODS:

A retrospective cross sectional 6 years study was done from November 2015 to October 2021.The study was conducted in the Histopathology section , Department of Pathology, MGM medical college & LSK hospital, Kishanganj. All the prostate specimens received for histopathological examination during the mentioned period were included in the study. All together 76 prostatic specimens were received.These were fixed in 10% neutral buffered formalin for 12 hours.After adequate fixation the specimens were submitted for processing.3 to 4 cassettes were prepared in each case, which accommodated 50% of total tissue, and weighed approximately 9 to 12 gms.Specimens weighing < 12gms were submitted entirely.[1]In general, random chips were submitted; however if some chips were firmer or had a yellow or yellow-orange appearance,they were preferentially submitted.Tissue processing was done with automated tissue processor and sections were made manually with microtome of thickness 2-4 microns.The slides were routinely stained with Hematoxylin and Eosin method[8] and examined under light microscope.Special staining was done wherever necessary.Theywere reported as per the histopathological findings and data thus collected were analysed. Carcinoma of the prostate cases were classified into different grades. Grading was based on glandular differentiation and the most commonly used Modified Gleason method was applied.

Immunohistochemistry is performed using a combination of microwave oven heating and standard streptavidin-biotin-peroxidase complex, using the Dako kit. Sections of human breast cancer tissue samples were used for positive controls.

III. RESULTS :

Altogether 76 histopathological specimens were analysed. Out of these, 60 cases (78.95%)were benign, 4 cases (5.26%) were pre-malignant and 12 cases (15.79%)were malignant.

Among these, 47 (61.84%) were Benign Prostatic Hyperplasia (BPH) [Fig 1.A],making it the commonest lesion. 11 (14.47%) were BPH with non specific prostatitis while 2 (2.63%) were BPH with granulomatous prostatitis [Fig 1.B].

BPH with Prostate Intraepithelial Neoplasia (PIN) was seen in 4 (5.26%) of the specimens. Low grade PIN(LGPIN) was seen in 3 cases and high grade PIN (HGPIN) [Fig 2] was seen in a single case.

Only 12 (15.79%) weremalignant [Table 1]. All the malignancies were adenocarcinomas [Fig 3]. All of them showed one or more of the different growth patterns and were categorized depending on the dominant growth pattern. The malignancies were graded using Modified Gleason's scoring system. Gleason's score is the sum of the primary and secondary patterns.

Pattern 3 is the most common primary pattern accounting to 6 cases (50%) and the Gleason's pattern 4 is the next most common pattern accounting to 4 cases (33.33%)

Pattern 4 is the most common secondary pattern accounting to 5 cases (41.67%) and the pattern 3 is the next most common pattern accounting to 4 cases (33.33%)

Gleason's score of 6 seen in 5 cases (41.67%). While, score 7 & 8 seen in 3 cases (25%) each and score 9 seen in 1 case (8.33%). [Table 2]

Immunohistochemistry was done in 12 cases of malignancy with adequate biopsy sample

In prostatic adenocarcinomas ER negative in all cases (0%), PR is positive in 5 cases (41.67%), AR is positive in all 12 cases (100%).[Fig 4, Fig 5& Table 3]

Most of the cases with Gleason's score 6 showed positive for PR accounting to 3/5 (60%).

The mean and median age of BPH was 69.2years and 68 years respectively, ranging from 54 to 80 years .The malignancies were seen after seventh decades.

IV. DISCUSSION

In the present study,the predominant lesion of prostatic specimens was BPH (61.84%).Pinky et al[1],Dhawan et al[9],Karkhuzhali et al[10] and Jehoram et al[11] in their studies observed similar findings of 72.6%, 86% , 83% and 93% respectively.

In our study,the mean& median age of BPH cases was 68.5 years &70years rangingfrom 54to 80 years.The mean age is comparable to a study by Pinky et al[1], Talukdar et al[12] and Cleary et al[13] with a mean age of 69.2 years, 67.7 years and 60 years respectively.

Non specific prostatitis accounted 14.47% of the prostatic lesions in the present study which is comparable to studies done by Pinky et al[1](15.07%)&Bal et al[14](11%).

Malignant lesions accounted for 15.79 % of the prostatic lesions in the present study.Similarfinding noted in the studies conducted by Bal et al[14] and Hamid et al[15](10% and 12.5% respectively).The risk of prostate cancer rises very steeply with age.Worldwide, about three-quarters of all cases occur in men aged 65 or more[16].In current study also, the malignancies were seen in the 7thdecades onwards.

The incidence of PIN in the present study was5.26 % which is similar(5.47%) to a study done by Pinky et al[1].

In the present study, Gleasons score 6 (moderately differentiated)was seen in 17 cases (35.41%). Similar observations are made in the studies of Micheal A Bean etal[17] accounting for 49%.

The earlier patterns of Gleason's score were not seen in our study, as compared with study done by Babaian Richard etal[18].

Gleason's scores 2 and 3 are only exceptionally assigned, because Gleasons pattern 1 is unusual. Gleason's score 4 is also relatively uncommon because pattern 2 is usually mixed with some pattern 3 resulting in a Gleason's score 5. Gleason's score 2-4 tumour may be seen in TURP material sampling the transitional zone. However in core needle biopsy material, it has been proposed that a Gleason's score of 2-4 should not be assigned[19,20].

In present study,estrogenreceptor (ER) expression was negative in tumour cells in all cases of prostatic adenocarcinoma regardless of Gleason's pattern. However 2 cases showed ER positivity in stromal cells. Similar observations are found in the study done by Wernert et al[21]. They concluded that estrogens do not act directly on prostatic carcinoma but inhibit growth via the hypophyseal-testicular axis. This observation may have clinical implications as tumor cells expressing these proteins are potentially estrogen responsive and will survive in an androgen-deprived situation and also if there is any need for treating the cancer with anti-estrogens or not.

In present study, out of 12 cases of prostatic adenocarcinomas with adequate tissue material, 5 cases (41.67%) were positive for PR expression with varying staining intensity. Among these, 3 cases (60%) with Gleason's score 6 showed intense positivity in 20-30% of the cells, 1 case (20%) with Gleason's score 7 showed mild to moderate positivity in 30-40% of the cells, 1 case (20%) with Gleason's score 8 showed mild positivity in 10% of cells.

All the 12 cases with adequate biopsy material in our study were positive for AR expression with varying staining intensity. Most of these cases showed strong positive AR expression in 80-90% of the tumour cells. So, in prostatic carcinoma cases the tumour cells showed highest content of AR expression than the other steroid hormone receptor expression.

In present study, AR immunoreactivity was almost exclusively nuclear and was observed in most of the tumor cells. Mean percentages of Androgen Receptor (AR) positive cells were significantly higher compared to other sex steroid receptors like Estrogen receptor (ER) and Progesterone receptor (PR).

V. CONCLUSION

From present study concluded that Benign Prostatic hyperplasia was the most common prostatic lesion occurring commonly after the age of 60 years. The commonest age group of presentation of both carcinoma and BPH was seen after 6th decades. Prostatic carcinoma relative less common than BPH, but when diagnosed histopathologicallyall cases of prostatic adenocarcinoma should be meticulously graded according to Gleason's scoring system as prognosis depends on Gleason's score. Immunohistochemistry should be done with regard to sex steroid receptor status and also supports the view that anti-androgen and anti-progesterone therapy is helpful in the treatment of prostatic adenocarcinoma.

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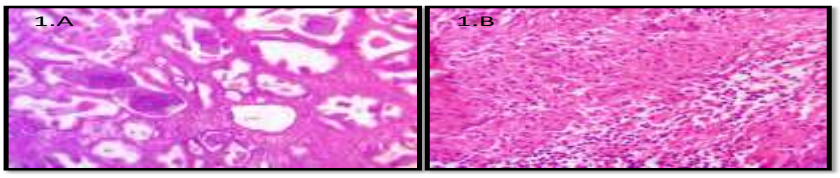
Figures and Tables:

Fig 1.A showing BPH , Fig 1.B showing granulomatous prostatitis (H&E stain, 40X)



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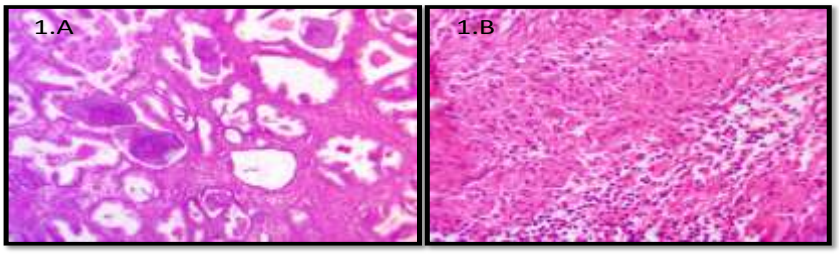

Fig 2. showing high grade PIN, Fig3. showing prostatic adenocarcinoma (H&E stain, 40x)

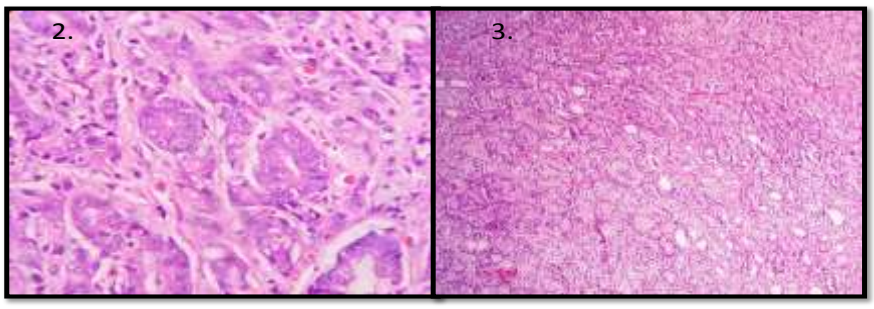

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Fig 4. showing PR expression in prostate cancer, Fig 5. showing nuclear AR staining in prostate cancer (DAB, 20x)

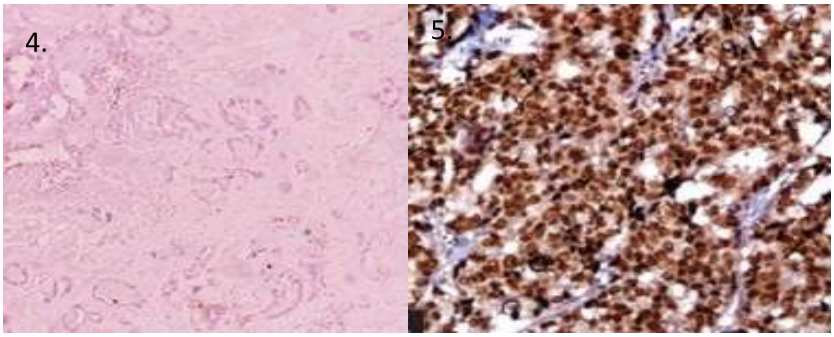

Table1: Microscopic findings of different prostatic lesions

Sl. No.	Microscopic findings	Cases
1.	BPH	47 (61.84%)
2.	Chronic Nonspecific Prostatitis	11 (14.47%)
3.	Granulomatous Prostatitis	2 (2.63%)
4.	PIN	4 (5.26%)
5.	Prostatic Adenocarcinoma	12 (15.79%)
Total		76 (100%)

Table 2: Gleason's scoring of prostatic carcinoma

SL. No.	Gleason's score	Cases
1.	6	5 (41.67%)
2.	7	3 (25%)
3.	8	3 (25%)
4.	9	1 (8.33%)
Total		12 (100%)