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Original Research Article

Histomorphological spectrum of prostatic lesions: A prospective study on TURP specimens by using immunohistochemical marker P504S

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Abstract

Aims and Objective: To study the histomorphological spectrum of non-neoplastic and neoplastic lesions of the Prostatic TURP specimens and analyse the utility of immunohistochemical marker P504S in various lesions of prostate.
Methods: This two-year prospective study on 65 transurethral resection specimens of prostate, was carried out in the Department of pathology, Dr B R Ambedkar Medical College, Bangalore. Immunohistochemical marker P504S was used and its expression in various lesions was analysed.
Results: Out of 65 cases studied, 52 (80%) were benign prostatic hypertrophy (BPH), 3 (4.6%) were non-specific granulomatous prostatitis, 1(1.5%) was prostatic abscess, 7(10.8%) were prostatic adenocarcinoma, 1(1.5%) case was urothelial carcinoma and 1 case (1.5%) had both prostatic adenocarcinoma and urothelial carcinoma. Low grade PIN was identified in 8 (12.3%) cases and all of these were associated with BPH. High grade PIN was seen in 9 (13.8%) cases and 7 of them were associated with adenocarcinoma. P504S marker was positive in all (100%) adenocarcinoma and 8 cases (88.9%) of High-grade PIN. Benign glands in BPH was negative for P504S.
Conclusion: BPH is the most common lesion of the prostate in the elderly and adenocarcinoma is the commonest type of prostatic carcinoma. P504S is of great value in differentiating HGPIN and malignant glands from benign glands.

Keywords: Benign prostatic hyperplasia, high grade PIN, adenocarcinoma, urothelial carcinoma

Introduction

Prostate is fibro musculo glandular organ encircling the neck of the urinary bladder. So, enlargement of prostate due to various lesions may give rise to bladder outlet obstruction [1].

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The most commonly encountered lesions of prostate in clinical practice are Benign prostatic hyperplasia, prostatic cancer and prostatitis [2]. Nodular hyperplasia of the prostate originates almost exclusively in the inner aspect of the prostate gland (transition zone).
The prevalence of BPH about 8% during the fourth decade, but it reaches 50% in the fifth decade and 75% in the eighth decade [3]. The spectrum of chronic prostatitis includes chronic bacterial, chronic abacterial and granulomatous prostatitis. Clinical features of chronic prostatitis are frequency, urgency, dysuria, hemato spermia and pain in lower back [4]. Prostatic intraepithelial neoplasia (PIN) is characterized as a neoplastic transformation of the lining epithelium of prostatic ducts [5]. Prostate cancer is the second most common cancer in men with a world incidence of 25.3 per 100,000 [6]. The number of cases has continuously increased over the past decades, partly due to the higher life expectancy. Using a highly specific antibody (P504S) directed against the enzyme AMACR**,** Jiang *et al*. found that strong immuno staining for the enzyme was present in prostatic carcinoma and in high-grade prostatic intraepithelial neoplasia [7].

Aims and Objectives

1) To study the histomorphological spectrum of non-neoplastic and neoplastic lesions of the Prostate in TURP specimens.
2) To analyse the utility of immunohistochemical marker P504S in various lesions of prostate.

Materials and Methods

This is a two-year prospective study conducted in the Department of Pathology, Dr BR Ambedkar Medical College, Bangalore. A total of 65 TURP specimens were included in this study. The clinical details of the patients were collected from the requisition form at Dr B R Ambedkar Medical Hospital. All the TURP specimens were fixed in 10% formalin and then the entire specimen was submitted for standard processing.5-micron thick tissue sections were taken from each block and was routinely stained with H&E. P504S immuno marker was done wherever necessary. Cellular localization of P504S is granular and cytoplasmic. Positive control used was Prostate cancer slide.

Observation and Results

Table 1: Distribution of cases according to Histopathological Diagnosis

HP Diagnosis	Frequency	Percentage (%)
Adenocarcinoma	7	10.8
BPH	52	80.0
NSGP	3	4.6
Prostatic abscess	1	1.5
Urothelial carcinoma	1	1.5
Adenocarcinoma + Urothelial carcinoma	1	1.5
Total	65	100.0

Table 2: Age wise distribution of cases according to Histopathological Diagnosis

Histopathological diagnosis	Age					Total
	40-49 yrs	50-59 yrs	60-69 yrs	70-79 yrs	80-89 yrs	
Carcinoma	0	0	1	3	5	9
(Adenocarcinoma + Urothelial Carcinoma)	0.0%	0.0%	11.1%	33.3%	55.6%	100.0%
BPH	2	9	21	12	8	52

	3.8%	17.3%	40.4%	23.1%	15.4%	100.0%
NSGP	0	1	2	0	0	3
	0.0%	33.3%	66.7%	0.0%	0.0%	100.0%
Prostatic abscess	0	0	1	0	0	1
	0.0%	0.0%	100.0%	0.0%	0.0%	100.0%
Total	2	10	25	15	13	65
	3.1%	15.4%	38.5%	23.1%	20.0%	100.0%

Table 3: Distribution of Prostatic Adenocarcinoma according to Gleason's Grading System

Gleason Score	Frequency	Valid Percent
5	1	12.5
7	1	12.5
8	2	25.0
9	3	37.5
10	1	12.5
Total	8	100.0

Table 4: Distribution of Prostatic Adenocarcinoma cases based on Tumour quantification

Tumour quantification	Frequency	Percentage (%)
<5%	1	12.5
>5%	7	87.5
Total	8	100.0

Table 5: Expression of P504S immunostaining in different cases

Type of case	IHC- P504S stain		Total
	Positive	Negative	
HGPIN	8	1	9
	88.9%	11.1%	100.0%
Adenocarcinoma	8	0	8
	100.0%	0.0%	100.0%
BPH	0	52	52
	0.0%	100.0%	100.0%

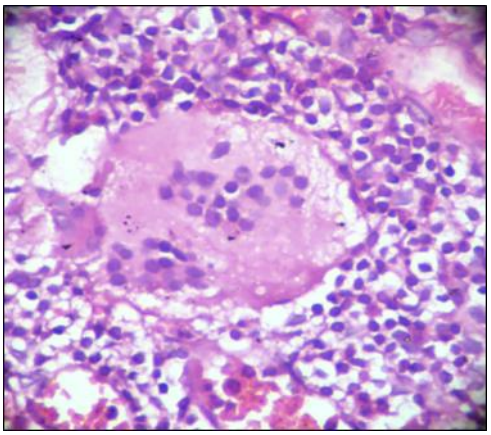

Fig 1: Non-specific granulomatous prostatitis showing multinucleated giant cell and histiocytes (40x)

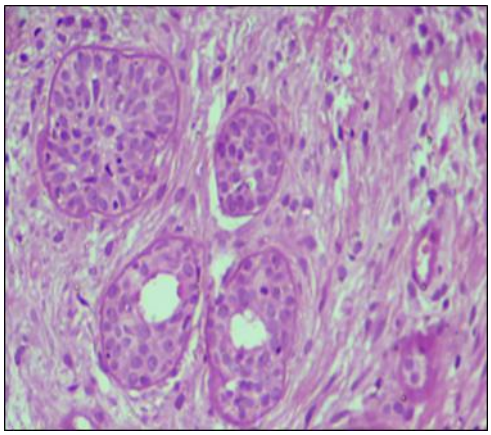

Fig 2: Basal cell hyperplasia (10x)

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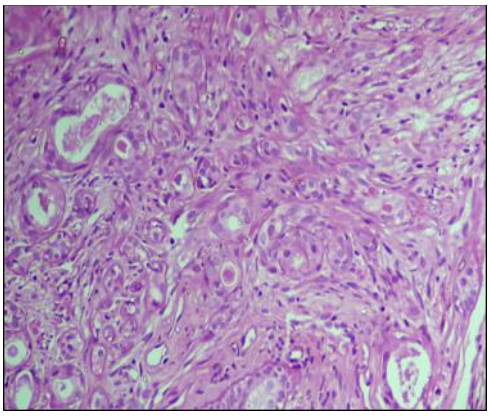

Fig 3: Adenocarcinoma-Gleason's Grade 2(10x)

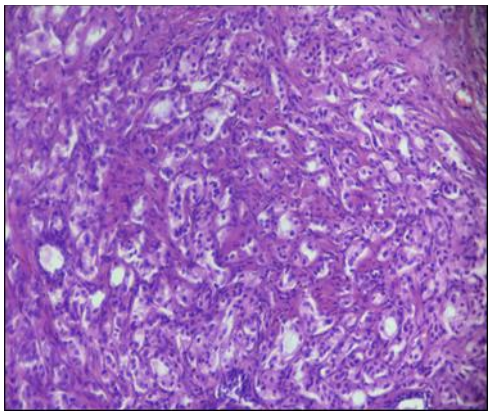

Fig 4: Adenocarcinoma-Gleason's Grade 3(10x)

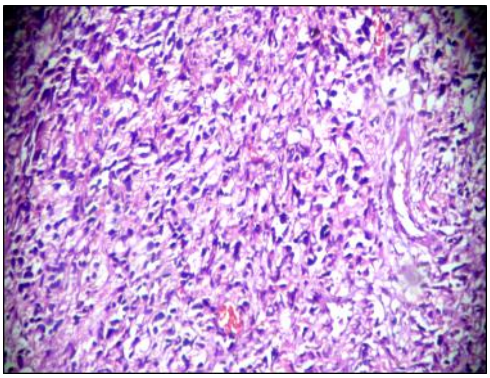

Fig 5: Adenocarcinoma -Gleason's grade 5(10x)

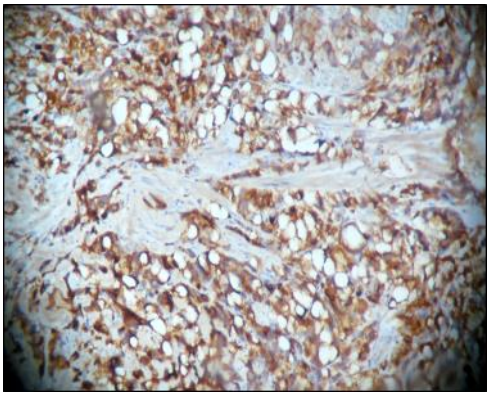

Fig 6: Adenocarcinoma showing strong cytoplasmic P504S positivity (40x)

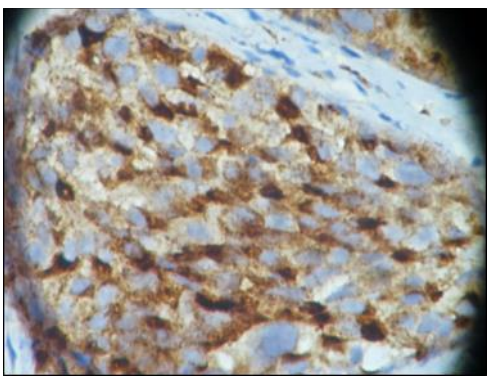

Fig 7: Urothelial carcinoma is positive for P504S stain (40x)

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A total number of 65 cases were studied. The cases were distributed in the age group of 45-85 years. The maximum number of patients were in the age group of 60-69 yrs. Out of 65 cases, 52 were benign prostatic hypertrophy (BPH), 3 were non-specific granulomatous prostatitis, 1 was prostatic abscess, 7 were prostatic adenocarcinoma, 1 case was urothelial carcinoma and 1case had both prostatic adenocarcinoma and urothelial carcinoma. Prostatic Intraepithelial Neoplasia was observed in 17 cases. Low grade PIN was seen in 8 cases of BPH. High grade PIN was seen in 9 cases, out of which 7 were seen in association with adenocarcinoma (Table 1, 2). Miscellaneous features like cystic atrophy, chronic non-specific prostatitis, stromal nodule, basal cell hyperplasia and transitional cell metaplasia were also seen associated with these lesions. Immunohistochemical marker P504S was done in the cases of BPH, Prostatic intraepithelial neoplasia, and carcinoma.

In the present study 3 (4.6%) cases of nonspecific granulomatous prostatitis and 1 (1.5%) case of prostatic abscess were identified out of 65 cases. Chronic non-specific prostatitis formed majority among inflammatory lesions and predominantly it was seen in BPH cases and also in few cases of prostatic adenocarcinoma. The cases of non-specific granulomatous prostatitis showed dense infiltrate of lymphocytes, plasma cells, foamy histiocytes and few multinucleated giant cells. Foci of glands showed destruction of epithelial lining.

There were totally 52 (80%) cases of BPH out of 65 cases. All these cases of BPH were in the age group of 45-85 yrs. The peak incidence was observed in the age group of 60-69 yrs. The mean age of BPH in this study belongs to 66.88 yrs. In all the 52 cases of BPH, the glands were negative for the P504S immunostaining. The percentage of negativity was 100%.

Basal cell hyperplasia was identified in 6 cases out of 65 cases. There were two patterns of basal cell hyperplasia identified. The complete basal cell hyperplasia showed solid nests of basal cells without central lumen and the incomplete form showed small lumina lined by secretory cells with clear cytoplasm and these are surrounded by multiple layers of basal cells. These basal cells were negative for P504S stain.

Foci of transitional cell metaplasia was seen in 4 cases of BPH. Low grade PIN was identified in 8 (12.3%) cases and all of these were associated with BPH. High grade PIN was seen in 9 (13.8%) cases and 7 of them were associated with adenocarcinoma. Out of 9 cases of HGPIN, 8 (88.9%) cases showed moderate to strong positivity which was cytoplasmic and circumferential and 1(11.1%) case was negative for P504S immunostaining.

In this present study there were 7 (10.8%) cases of Adenocarcinoma, 1 (1.5%) case of Adenocarcinoma with Urothelial carcinoma and 1 (1.5%) case of Urothelial carcinoma out of 65 cases identified. All the 9 malignant lesions constituted 13.8% of cases. Malignant lesions in the age group of 60-69 yrs, 70-79 yrs, 80-89 yrs were constituting 1 (11.1%) case, 3 (33.3%) cases, 5 (55.6%) cases respectively. The peak incidence was seen in 9th decade. The mean age of malignant cases was 76.78 yrs. The gleason score 5,7,8,9,10 constituted 1 (12.5%) case, 1 (12.5%) case, 2(25%) cases, 3 (37.5%) and 1 (12.5%) case respectively (Table 3). Majority of patients diagnosed as conventional adenocarcinoma had graded as score 9 (3cases, 37.5%) followed by score 8 (2 cases, 25%). 1 (12.5%) case of adenocarcinoma showed < 5% and remaining 7 (87.5%) cases showed >5% of tumour quantification (Table 4). All the 8 cases of adenocarcinoma showed strong cytoplasmic, granular positivity. The percentage of positivity was 100% (Table 5).

There were 2 cases of urothelial carcinoma found in this study and both were in 9th decade of age (81 and 85 years old). One of that case was associated with adenocarcinoma. Both the cases showed strong cytoplasmic positivity for P504S stain.

Interpretation of P504S staining

Positive staining pertains to dark diffuse or granular, cytoplasmic or luminal, but circumferential. The percentage positivity was graded from 0+ to 3+ as follows:

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0% cells - 0+, negative.
1-10% cells - 1+, mild.
11-50% cells - 2+, moderate.
> 51% cells - 3+, strong.

Discussion

The present study was carried out on 65 cases of TURP specimens. Among the inflammatory lesions, chronic prostatitis formed majority of cases and was seen associated with BPH. Non-specific granulomatous prostatitis was identified in 4.6% (3 cases) of cases. Herranz *et al.* [8] showed in their study that 1.5% (11 cases) of patients had nonspecific granulomatous prostatitis. Out of 65 TURP specimens BPH was diagnosed in 52 (80%) of cases and it was the major type of lesion found in this study. This was comparable with studies done by Djavan *et al.* [9] (83%) and Pacelli and Bostwick [10] (81.7%). All these cases of BPH were in the age group of 45-85 years. The peak incidence was observed in the age group of 60-69 years. Jasani *et al.* [11] showed in their study the age wise distribution as, 3.92% below 50 years, 96.08% at 51-70 years and no cases were found above 70 years. In the present study the age incidence was 7.8% below 50 years, 59.6% at 51-70 years and 32.6% above 70years. the mean age of BPH patients was 66.88 years. It is comparable with the study done by Mwakyoma HA [12]. In all the 52 (100%) cases of BPH, the glands were negative for the P504S immunostaining. Similar findings observed by Jiang *et al.* [13] (91.7%) and Kumaresan *et al.* [14] (100%).
12.3% (8 cases) of low-grade PIN and 13.8% (9 cases) of high-grade PIN were identified. The incidence of High-grade PIN different studies are, Gaudin *et al.* [15] (3.2%) and Skjorten *et al.* [16] (33%). The present study showed moderate to strong positivity for P504S stain in 8 (88.9%) cases of HGPIN and 1 (11.1%) case was negative. This finding is comparable to Wu *et al.* [17] (90%), Yu *et al.* [18] (91.67%) and Kunju *et al.* [19] (89%). There were 8 (12.3%) cases of adenocarcinoma out of 65 TURP specimens identified. Of these 1 case was associated with urothelial carcinoma. All the 9 (100%) cases (adenocarcinoma and urothelial carcinoma) were seen above 65 years. The peak incidence was seen in 9th decade. The mean age was 76.78 years. Xie *et al.* [20] found in their study that the percentage of carcinoma prostate was 84.2% over 65 years of age. Shimada *et al.* [21] found 75% of carcinoma prostate above 65 years. This variation in age incidence could be due to variation in sample size.
The distribution of patients in the present study was 0%, 25% and 75% in Gleason's score of 2-4, 5-7 and 8-10 respectively. Mwakyoma and Mabandi [22] in their study showed the distribution of patients were 5.3%, 61.1% and 33.6% in Gleason's score of 2-4, 5-7 and 8-10 respectively. Divrik *et al.* [23] observed in their study that the distribution of patients were 9.7%, 76.7% and 13.6% in Gleason's score of 2-4, 5-7 and 8-10 respectively. The present study showed more number of patients in Gleason's score 8-10. All the 8 cases (100%) of adenocarcinoma showed strong positivity to P504S stain. Similar findings observed by Jiang *et al.* [24] (100%), Yu *et al.* [18] (100%) and Rubin *et al.* [25] (97%).
There were 2 cases of urothelial carcinoma found in this study and both were in 9th decade of age. Both the cases showed positivity for P504S stain. Beach *et al.* [26] found 5 (83%) out of 6 cases of invasive urothelial carcinoma showed P504S positivity.

Conclusion

BPH is the most common lesion of the prostate in the elderly. Chronic nonspecific prostatitis is the commonest inflammatory condition of the prostate and granulomatous prostatitis is rarely encountered. Conventional adenocarcinoma is the commonest type of prostatic

carcinoma. P504S is of great value in differentiating HGPIN and malignant glands from benign glands. Determining the frequency of various lesions of prostate especially precursor lesions would help in the patient follow up and reduce the morbidity and mortality. Hence thorough histopathological examination is gold standard which would help in arriving at a confirmatory diagnosis for the better treatment of the patient.

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