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A Histomorphological Study of Prostatic Turp Specimens with Special Reference To Prostatic Intraepithelial Neoplasia by Using Immunohistochemistry

KEYWORDS: prostrate, TURP, Benign prostatic hyperplasia, prostatic intraepithelial neoplasm, prostatic adenocarcinoma, urothelial carcinoma, p63, p504S, AMACR.

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ABSTRACT

AIMS AND OBJECTIVES

To study the histomorphological spectrum of non-neoplastic and neoplastic lesions of the Prostate in TURP specimens. To know the incidence of Prostatic Intraepithelial Neoplasia in TURP specimens. To study the association of Prostatic Intraepithelial Neoplasia in different prostatic lesions. To find out the expression of immunohistochemical markers, p63 and P504S (AMACR) in BPH, Prostatic intraepithelial neoplasia and Carcinoma cases.

MATERIAL AND METHODS

This is a 4 years (2 year retrospective, 2 years prospective) study which includes 130 cases, i.e., from august 2011 to july 2015 at Mahatma Gandhi Memorial Hospital, Kakatiya Medical College, Warangal. All the 130 cases were TURP specimens.

RESULTS

A total number of 130 cases were studied. The cases were distributed in the age group of 45–85 yrs. The maximum number of patients were in the age range of 60-69 yrs. Out of 130 cases, 104(80%) were Benign prostatic hyperplasia(BPH), 6(4.6%) were non-specific granulomatous prostatitis(NSGP), 2(4.6%) were prostatic abscess, 2(1.5%) were basal cell hyperplasia, 14(10.8%) were prostatic adenocarcinoma, and 2(1.5%) cases had both prostatic adenocarcinoma and urothelial carcinoma. Foci of Low grade prostatic intraepithelial neoplasm (LGPIN) was identified in 16(12.3%) cases. All the LGPIN foci were associated with BPH. High grade prostatic intra epithelial neoplasm (HGPIN) was identified in 18(13.8%) cases. Out of these 4(3.8%) HGPIN foci were seen in BPH and 14(87.5%) were seen associated with adenocarcinoma. 4 microscopic patterns identified in HGPIN usually with multiple patterns in each case. The percentage of tufting, flat, micropapillary and cribriform patterns were 66.7%, 55.6%, 33.3% and 11.1% respectively.

BPH showed 100% positivity for p63 stain and 100% negativity for P504S stain. HGPIN showed 100% positivity for p63 stain and 88.9% positivity for P504S stain. All the cases of adenocarcinoma showed negativity for p63 stain. 100% positivity was seen for P504S stain in adenocarcinoma. Both the cases of urothelial carcinoma showed positivity for p63 and P504S staining.

CONCLUSION

BPH is the most common lesion of the prostate in the elderly. Conventional adenocarcinoma is the commonest type of prostatic carcinoma. HGPIN has a high degree of association with prostatic carcinoma. Basal cell marker p63 is really helpful in differentiating benign and HGPIN glands from malignant glands. P504S is of great value in differentiating HGPIN and malignant glands from benign glands.

INTRODUCTION

Prostate cancer is a leading cause of morbidity and mortality worldwide. PIN and Atypical Adenomatous Hyperplasia (AAH) are now considered to be the most common precursors of prostate cancer. AAH is usually a microscopic finding, but PIN can only be diagnosed by histopathological examination. It is impossible to detect PIN by digital rectal examination, Prostate Specific Antigen assay (PSA) or ultrasound. In view of increasing trend of the occurrence of both neoplastic and non neoplastic lesions of the prostate, the current study aims at evaluating the histomorphological features of Transurethral Resection specimens (TURP) of prostate according to ISUP 2010 guidelines, with special reference to PIN, for a period of 3 years by using of immunohistochemical markers and to develop therapeutic strategies.

METHODOLOGY

This is a 4 years (2 year retrospective, 2 years prospective) study which includes 130 cases, i.e., from august 2011 to july 2015 at MAHATMA GANDHI MEMORIAL HOSPITAL, Kakatiya Medical College, Warangal. All the 130 cases were TURP specimens. The clinical history and the details of the patient were collected from the requisition forms.

For light microscopy one slide from each block was routinely stained with H&E to arrive at a diagnosis. Immunohistochemical staining was done for p63 and p504S markers in BPH,PIN and carcinoma .Normal prostrate is taken as a positive control.

OBSERVATIONS AND RESULTS

A total number of 130 cases were studied. The cases were distributed in the age group of 45–85 yrs. The maximum number of patients were in the age range of 60-69 yrs. Out of 130 cases, 104(80%) were Benign prostatic hyperplasia(BPH), 6(4.6%) were non-specific granulomatous

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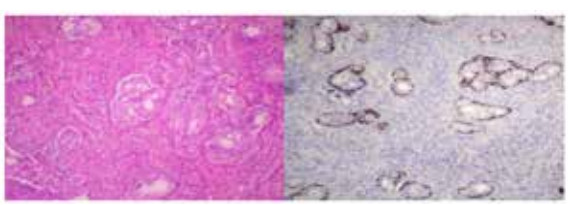
prostatitis(NSGP), 2(4.6%) were prostatic abscess, 2(1.5%) were basal cell hyperplasia, 14(10.8%) were prostatic adenocarcinoma, and 2(1.5%) cases had both prostatic adenocarcinoma and urothelial carcinoma. Foci of Low grade prostatic intra epithelial neoplasm (LGPIN) was identified in 16(12.3%) cases. All the LGPIN foci were associated with BPH. High grade prostatic intra epithelial neoplasm (HGPIN) was identified in 18(13.8%) cases. Out of these 4(3.8%) HGPIN foci were seen in BPH and 14(87.5%) were seen associated with adenocarcinoma. 4 microscopic patterns identified in HGPIN usually with multiple patterns in each case. The percentage of tufting, flat, micropapillary and cribriform patterns were 66.7%, 55.6%, 33.3% and 11.1% respectively. Cystic atrophy, chronic non-specific prostatitis, stromal nodule and transitional cell metaplasia were also seen associated with these lesions. Chronic non-specific prostatitis formed majority among inflammatory lesions and predominantly it was seen in BPH cases and also in few cases of carcinoma. IHC was done using p63 and P504S markers in the cases of BPH, PIN, and carcinoma.

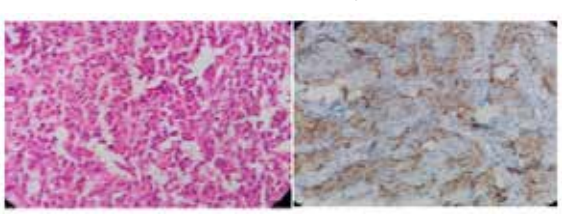
Expression of p63 immunostaining : Of 104 cases of BPH complete positivity was seen in all of the cases. Of 18 cases of HGPIN complete positivity was seen in 16(88.9%) cases and 2(11.1%) case showed partial positivity. Of 16 cases of adenocarcinoma 100% of cases showed complete negativity. Of 2 cases of basal cell hyperplasia both showed 100% positivity. Both the cases of urothelial carcinoma showed positivity.

Picture 1: Microscopy of HGPIN H&E staining and p63 immunostaining



Espression of p504S immunostaining : Of 104 cases of BPH 100% showed complete negativity. Of 18 cases of HGPIN 16 (88.9%) cases showed moderate to strong positivity which was cytoplasmic and circumferential and 2 (11.1%) case showed negativity. Of 16 cases of adenocarcinoma 100% of cases showed complete positivity. Of 2 cases of basal cell hyperplasia both showed 100% negativity. Both the cases of urothelial carcinoma showed strong cytoplasmic positivity.

Picture 2: Microscopy of adenocarcinoma H&E staining and p504S(AMACR) immunostaining



Gleason's Grading system: The Gleason score 5,7,8,9 and 10 constituted 2 (12.5%) cases, 2 (12.5%) cases, 4 (25%) cases, 6 (37.5%) and 2 (12.5%) cases respectively. Majority of patients with adenocarcinoma had graded as score 9 followed by score 8.

Tumour quantification: 2 (12.5%) cases of adenocarcinoma showed < 5% and remaining 14 (87.5%) cases showed >5% of tumour quantification.

Table 1: Expression of p63 & p504S immunostaining in the present study(about here)

Diagnosis	p63 Number of cases (percentage)			p504S Number of cases (percentage)	
	Positive		Negative	Positive	Negative
	complete	partial			
BPH	104 (100%)	0	0	0	104(100%)
HGPIN	16(88.9%)	2 (11.1%)	0	16(88.9%)	2(11.1%)
Adenocarcinoma	0	0	16 (100%)	16(100%)	0
Urothelial Ca	2 (100%)	0	0	2(100%)	0

DISCUSSION

The present study was carried out on 130 cases of TURP specimens. The specimens were examined for analyzing various histomorphological lesions of prostate, with special emphasis given to prostatic intraepithelial neoplasia. There were 2 immunohistochemical markers (p63, P504S) used in benign, prostatic intraepithelial neoplasia and malignant cases.

Among the inflammatory lesions, chronic prostatitis formed majority of cases and was seen in associated with BPH. Non specific granulomatous prostatitis was identified in 6 cases (4.6%). Herranz et al[10] showed in their study that 11 cases (1.5%), showed nonspecific granulomatous prostatitis. In present study the percentage is slightly higher.

In the benign proliferative lesions, BPH was the major type of lesion found in this study. Incidence of BPH is correlated with Pacelli and Bostwick[1] study. 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. In the present study the mean age of BPH patients was 66.88 yrs. It is comparable with the study done by Mwakyoma HA[11]. p63 positivity in BPH is correlated with Kruslin et al[3] study. P504S negativity in BPH is correlated with Kumaresan et al[9] study.

The present study showed 16 cases of LGPIN associated with BPH and no LGPIN case was seen in adenocarcinoma. 15.4% of BPH cases showed LGPIN in this study. Rekhi et al[2] found LGPIN in 18.6% cases of BPH and 5.8% of cases of adenocarcinoma. HGPIN was observed in 3.8% of the cases of BPH and 87.5% of the cases of adenocarcinoma. 4 microscopic patterns identified in HGPIN the commonest pattern was tufting type followed by flat type. Bostwick et al[12] in their study found the percentage of tufting, flat, micropapillary and cribriform patterns 87%, 28%, 85% and 32% respectively. The commonest pattern was tufting type followed by micropapillary type. In the present study positivity for p63 staining is comparable to Kruslin et al[3] who showed 100% positivity for p63 in 28 HGPIN cases. Positivity for P504S stain is comparable to Kunju et al[6] with 89% positivity.

In present study all the (100%) cases carcinomas were seen above 65 yrs. The peak incidence was seen in 9th decade.

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The mean age was 76.78 yrs comparable to Mwakyoma HA[11] which is 75.6. Incidence of adenocarcinoma is 12.3%. Distributin of Gleason score in majority of caases is 8-10 that is 75% which is greater than other studies.

In adenocarcinoma p63 negativity is similar to other studies Molinie et al[7] , Shah et al[4] and Ud din et al[5] . P504S positivity is similar to Jiang et al[13], Yu et al[8] and Yang et al[14]. Langner et al[15] performed p63 stain in 53 urothelial carcinoma and found positivity in 51 (96.2%) cases. In the present study both the cases showed positivity for p63 stain. Beach et al[16] found 5 (83%) out of 6 cases of invasive urothelial carcinoma showed P504S positivity. In the present study both the cases showed strong cytoplasmic positivity for P504S stain.

CONCLUSION

From the above study it can be concluded that - BPH is the most common lesion of the prostate in the elderly. Chronic nonspecific prostatitis is the commonest inflammatory condition of the prostate. Granulomatous prostatitis is rarely encountered. Conventional adenocarcinoma is the commonest type of prostatic carcinoma. Gleason's score of 8-10 is the most common score in adenocarcinoma of prostate. HGPIN has a high degree of association with prostatic carcinoma. This reflects a greater possibility of HGPIN as a precursor lesion to carcinoma prostate. Basal cell marker p63 is really helpful in differentiating benign and HGPIN glands from malignant glands. P504S is of great value in differentiating HGPIN and malignant glands from benign glands. In view of high degree of association of HGPIN with prostatic carcinoma, it is suggested that these HGPIN patients need close follow-up, observations and investigations to rule out existence of carcinoma, especially in the peripheral zone.

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