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Original Research Article

Histopathological Analysis of Prostatic Lesions and Comparing the Role of p63 and High Molecular Weight Cytokeratin (HMWCK) in Distinguishing Prostatic Carcinoma from Benign Prostatic Lesions and its Precursors

Kalpana B. Rathod[1], Dhanshri Kashinath Shinde[2], Jeetesh Vinayak Gaunkar[3], Leena Nakate[4], Shweta Jadhav[5]

[1]Associate Professor, Department of Pathology, B. J. Govt Medical College, Pune
[2]Senior Resident, Department of Pathology, B. J. Govt Medical College, Pune
[3]Senior Resident, Department of Pathology, B. J. Govt Medical College, Pune
[4]Professor and Head, Department of Pathology, B. J. Govt Medical College, Pune
[5]Assistant Professor, Priyadarshini JL College of Pharmacy, Nagpur

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Corresponding Author: Dr. Kalpana B. Rathod
Conflict of interest: Nil

Abstract:

Background: Prostate cancer is one of the leading causes of morbidity and mortality in elderly men throughout the world. There is a tendency to under diagnose small focus of prostatic adenocarcinoma or over diagnose benign lesions mimicking cancer. The application of immunohistochemistry using basal cell specific markers like p63 and high molecular weight cytokeratin (HMWCK) can help in distinguishing prostate cancer from its benign mimickers thus confirming the diagnosis especially in equivocal cases.

Aims: To study and compare the role of p63 and High Molecular Weight Cytokeratin (HMWCK) in distinguishing the prostatic carcinoma from its benign lesions and its precursors.

Settings and Design: Tertiary Health Care Centre based cross sectional study.

Material and Method: All cases of prostatic lesions received in the department of pathology in tertiary care center during the period of January 2019 to June 2020 were examined. Grossing and sectioning of the formalin fixed samples was done. Routine H & E staining and IHC immunostaining using P63 and HMWCK was done. Inadequate biopsies were excluded.

Statistical Analysis: Using SPSS Software.

Results and conclusion: Histopathological analysis of 115 prostatic lesions was done. The sensitivity of p63 was higher compared to HMWCK demonstrating that p63 is more sensitive in identifying the basal cells in non-malignant conditions. Both the immunohistochemical stains showed a very high specificity in the malignant lesions. The present study showed that immunohistochemistry using basal cell markers like HMWCK and p63 can be very significant to tackle diagnostic dilemmas in challenging cases and in premalignant conditions.

Keywords: IHC, HMWCK, P63.

Introduction

Prostate cancer is now the sixth most common cancer in the world (in terms of number of new cases) responsible for morbidity and mortality in elderly men throughout the world [1]. Genetic and epigenetic factors, along with influence of androgens play a role in development of benign prostatic hyperplasia and prostate cancer. The incidence of these prostatic lesions increase with advancing age [2].

There is a tendency to under diagnose small focus of prostatic adenocarcinoma or over diagnose benign lesions mimicking cancer [3] eg. Glandular atrophy, post-atrophic hyperplasia, adenosis (atypical adenomatous hyperplasia), sclerosing adenosis and radiation induced atypia. This study mainly aims at evaluating and comparing the sensitivity and specificity of HMWCK and p63 in distinguishing prostatic carcinoma from benign prostatic lesions.

The application of immunohistochemistry using basal cell specific markers like p63 and high molecular weight cytokeratin (HMWCK) can help in distinguishing prostate cancer from its benign mimickers thus confirming the diagnosis especially in equivocal cases.

Aims & Objectives

1. To calculate the occurrence of prostatic lesions in Tertiary care hospital during the period of January 2019 to June 2020.
2. To study and compare the role of p63 and High Molecular Weight Cytokeratin (HMWCK) in distinguishing the prostatic carcinoma from its benign lesions and its precursors.

Materials and Methods

Nature of study: Tertiary Health Care Centre based cross sectional study.

Sample size: All cases of prostatic lesions received in the department of pathology in tertiary care center during the period of January 2019 to June 2020.

Method:

Tissue specimen of all the cases having prostatic lesions was selected for the study. Grossing and sectioning of the formalin fixed samples was done.

Histopathology: For microscopy, detailed sectioning of the gross specimen was done. Entire biopsy was processed. In case of TUR specimen, 5 blocks or 12 grams of randomly selected chips were submitted. Standard-size sections were submitted in case of radical prostatectomy. The slides were stained with hematoxylin & eosin stain and evaluated. Paraffin blocks are preserved.

Immunohistochemistry: Staining with HMWCK and P63 was done and evaluated.

Inclusion Criteria: All cases of radical prostatectomy specimen, prostatic biopsies and TURP specimen.

Exclusion criteria: inadequate biopsies.

Statistical analysis:

This was a cross sectional study and statistical analysis was done by using SPSS Software wherever possible.

Result:

A total of 7764 histopathological specimens were received in the Dept. of pathology in the tertiary care centre from January 2019 to June 2020. Of these 115 cases (1.48%) constituted prostatic specimen.

Out of these, 89 were benign lesions (77.39%) as shown in figure number 1, 23 were malignant lesions (20.0%) as shown in figure number 2 and 3 were pre-malignant lesions (2.61%) ,as shown in chart number 1.

It is evident that all of the malignant glands showed absence of immunoreactivity towards HMWCK as well as p63. Thus the specificity of both the immunohistochemical stains is 100%. 5 cases showed negative immunoreactivity with HMWCK and 2 cases with p63. The sensitivity in identifying the basal cells was 94.56% for HMWCK and 97.82% for p63.

The result of our study thus demonstrates that p63 is more sensitive in identifying the basal cells in non-malignant conditions as evident from the statistical analysis.

The specificity however for both the immunohistochemical stains is very high in cases of prostatic carcinoma.

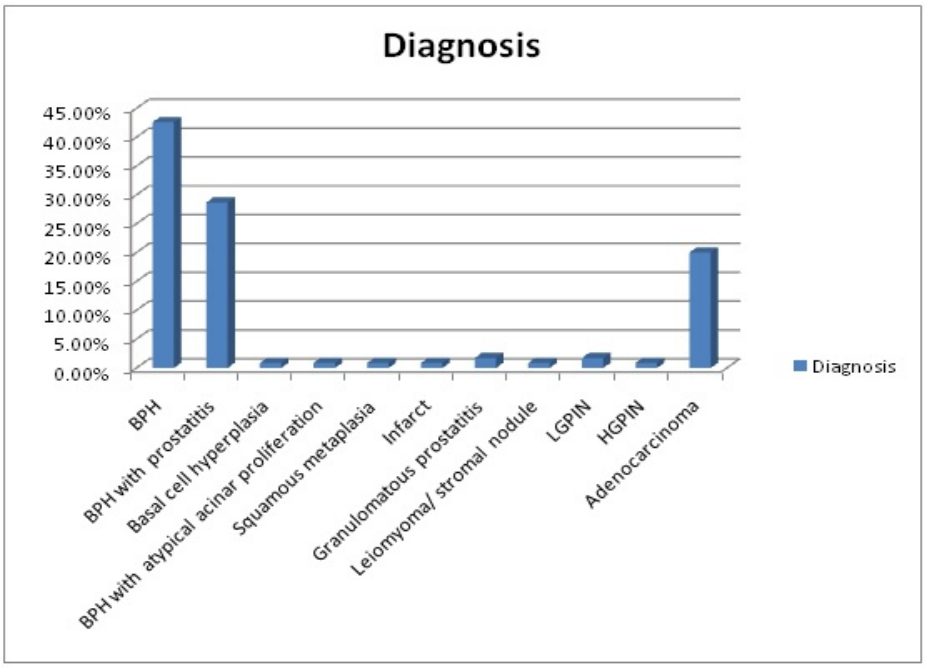

Chart 1: Final histopathological diagnosis

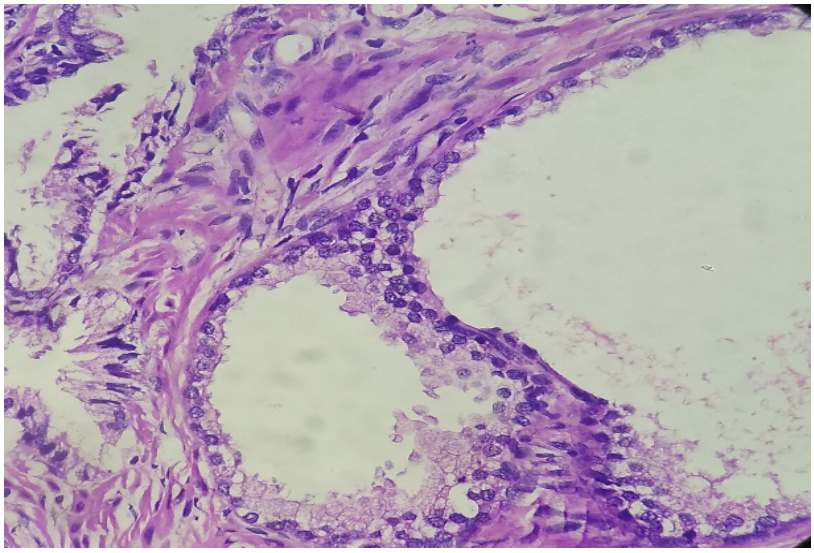

Figure 1: BHP H & E

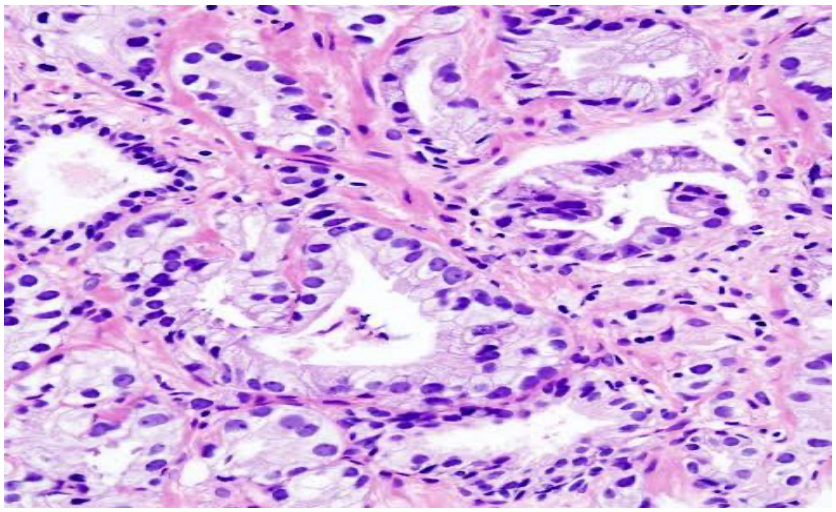

Figure 2: Prostatic Adenocarcinoma H & E

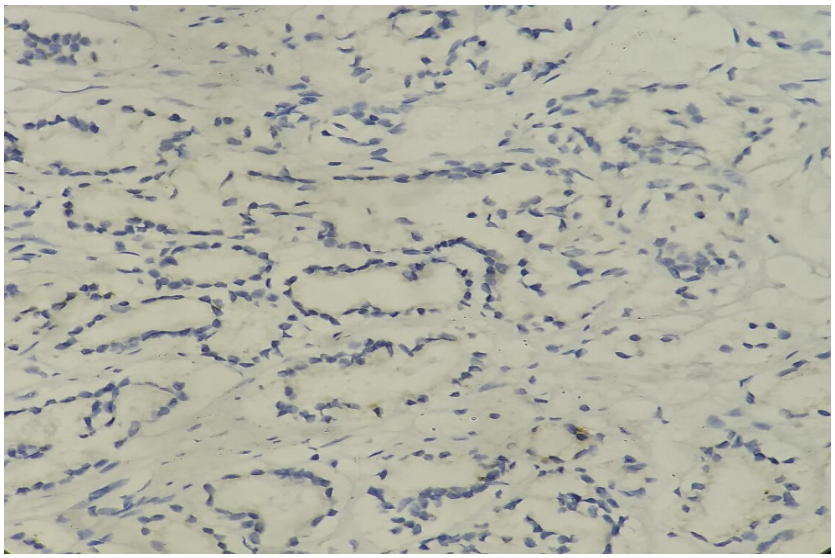

Figure 3: Prostatic Adenocarcinoma p63 immunostain

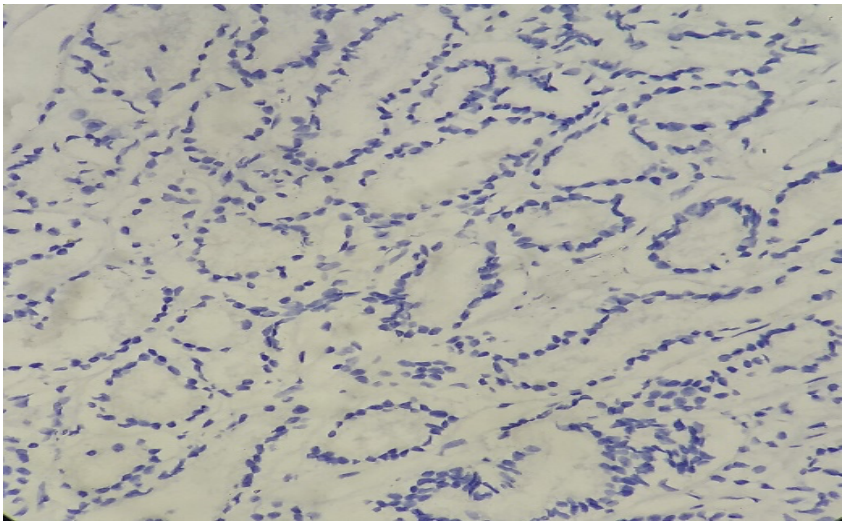

Figure 4: Prostatic Adenocarcinoma HMWCK immunostain

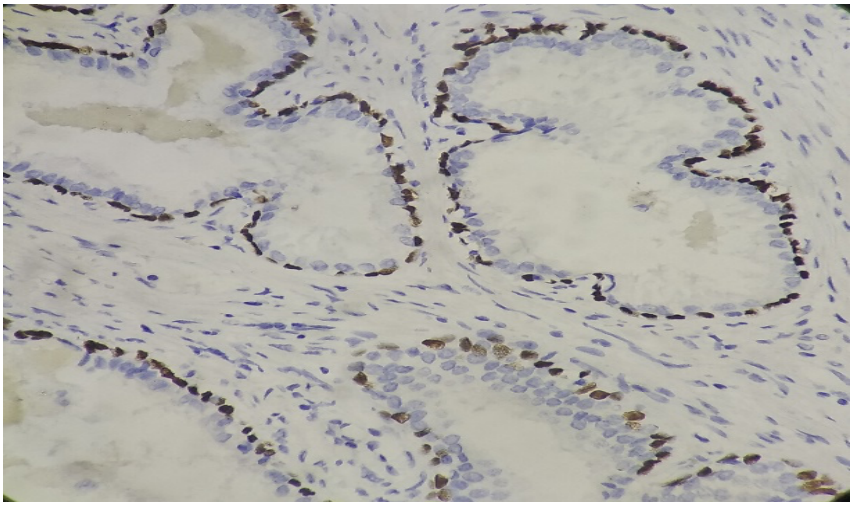

Figure 5: BHP p63 immunostain

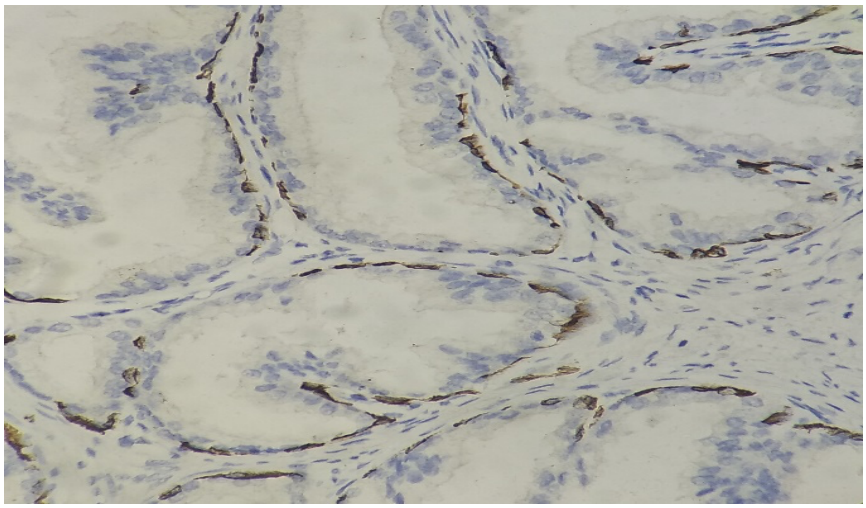

Figure 6: BHP HMWCK immunostain

Table 1: Results of HMWCK stain in non-malignant and malignant conditions

HMWCK	Non Malignant	Malignant	Total	P value
Positive	87	0	87	>0.05
Negative	5	23	28	
Total	92	23	115	

Table 2: Results of p63 stain in non-malignant and malignant conditions

p63	Non Malignant	Malignant	Total	P value
Positive	90	0	90	>0.05
Negative	2	23	25	
Total	92	23	115	

Discussion:

BPH and prostate cancer are commonly seen in elderly as its incidence increases with advancing age. The various histological appearances of BPH and that of the prostatic adenocarcinoma are well known and have been described and documented extensively in the literature. These two urologic conditions are not only common among elderly men; they also exhibit similar hormonal, epidemiologic and clinical factors. Both conditions increase with advancing age, requiring androgens for growth and development and thus responding to antiandrogenic therapy [4]. They also share similar risk factors such as insulin like growth factors, insulin and obesity [5].

This study was undertaken to evaluate the various histological lesions in the prostatic specimens and to evaluate the role of IHC in differentiating benign lesions from malignant lesions specially in diagnostically challenging cases. In this study, 115 prostatic lesions were analysed which accounted for 1.48% of the total surgical specimens received during the study period.

Immunohistochemistry:

Some suspicious (but not diagnostic) architectural or cytological features, especially in cases where there are only small foci of atypical glands, negative staining in the basal cells of the prostatic glands favours the diagnosis of adenocarcinoma.

Since p63 is expressed by the basal cells of prostate and is also essential for the prostate development, immunohistochemical staining for p63 has generated some interest. Signoretti et al highlighted the role of p63 in development of prostate and also its expression not only in the basal cell layer but also in subset of HMWCK negative cases as well[6].

In the present study, out of 23 cases of prostatic carcinoma, all the cases showed negative immunohistochemical staining for both p63 as well as HMWCK (100% specificity) as shown in table number 1,2 and figure number3,4. Out of the 92 cases including benign and premalignant conditions, HMWCK showed positivity in 87 cases whereas p63 showed positivity in 90 cases as shown in table number 1,2 and figure number 5,6. This absence of staining can be attributed to prolonged formalin fixation, as it can decrease the antigenicity of the immunohistochemical stains [7]. 1 case of the PIN showed negativity with both HMWCK and p63. This is correlated with studies done by Shah et al and Samundeeswari et al, who also reported absent basal cell layer staining with both HMWCK and p63.

This absence of expression can be due to diminished or absence of gene expression of the basal cell markers, technical variables including those resulting from surgical procedures or antigen retrieval methods. This was correlated with study done by Multhaupt et al wherein, there was a loss of antigenicity for HMWCK in 88% of the benign glands obtained by trans urethral resection if antigen retrieval was not used [8].

In one of the cases of adenocarcinoma, there was focal positivity for basal cells. Although the loss of basal cells was prominent in the malignant region, it served as an internal control.

In the present study, the sensitivity of HMWCK was 94.56 and that of p63 was 97.82 in identifying the basal cells in benign lesions. Hence p63 was more sensitive in identifying the basal cells as compared to HMWCK. This was comparable to study done by Shah et al and Samundeeswari et al, where p63 was found to be more sensitive than HMWCK giving more advantage to arrive at a diagnosis in challenging cases.

Conclusion:

The sensitivity of p63 was higher compared to HMWCK demonstrating that p63 is more sensitive in identifying the basal cells in non-malignant conditions.

Both the immunohistochemical stains showed a very high specificity in the malignant lesions.

The present study showed that immunohistochemistry using basal cell markers like HMWCK and p63 can be very significant to tackle diagnostic dilemmas in challenging cases and in premalignant conditions.

Cautery artefacts can impair the staining ability and interfere while reporting the lesions in TURP specimens hence staining with p63 appears slightly superior. The nuclear reaction is also easier to interpret than the cytoplasmic staining seen in HMWCK. The background staining is less in case of p63.

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