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The Role And Comparative Study of P63 And Hmwck In Prostatic Lesions.

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Abstract: *Immunohistochemical detection of basal cells is widely used to help in the diagnosis or exclusion of prostatic carcinoma in a diagnostically challenging cases. The objective of this study was at evaluating the role and comparing the sensitivity and specificity of HMWCK and p63 in prostatic lesions. This was a retrospective study carried out in our institution on 150 lesions. It was found that p63 is more sensitive than HMWCK in identifying the basal cells in diagnostically challenging cases.*
Keywords: *Gleason's grading, HMWCK , p63, Prostatic lesions.*

I. Introduction

Prostatic disease is responsible for significant morbidity and mortality in elderly men throughout the world. It is not uncommon to under diagnose small focus of prostaticadenocarcinoma or over diagnose benign lesions mimicking cancer. Though the diagnosis of prostatic carcinoma can be made on morphologic features and graded according to Gleason's grading, sometimes it can be challenging when pathologist are faced with certain problems such as limited tissue samples, small foci of carcinoma, technical problems like crush artifact and in benign mimickers. In such case, immunohistochemistry using basal cell markers like p63, HMWCK can be helpful.

II. Materials And Methods

This retrospective study was carried out in the department of pathology over 24 months. About 150 cases of prostatic lesions, including TURP and trucut biopsies were studied. All the specimens were fixed in 10 % neutral formalin and were subjected to histopathological examination. Sections of 2 - 4 micron thickness were made and routine staining with haematoxylin and eosin was done and looked for various lesions. Immunohistochemistry with basal cell specific markers like HMWCK (34βE12) and p63 was done for 12 cases including BPH, PIN, Benign mimickers like Basal cell hyperplasia, atrophy and prostatic adenocarcinoma. Statistical analysts was done to compare the role of HMWCK and p63 in these cases.

III. Results

Table I shows the result of following cases after being treated with HMWCK and p63 immunostaining. Table 2 shows the results of HMWCK staining in Benign, premalignant and malignant prostatic glands and inferred the Sensitivity of HMW-CK = 62.5 % Specificity of HMWCK = 100%.Similarly Table 3 shows the result of p63 staining in Benign , premalignant and malignant prostatic glands and inferred the sensitivity of p63 to be 87.5%, Specificity of p63 to be 100%

From Table 1 & 2 it is apparent that all of the malignant glands showed total absence of HMW- CK and p63 staining leading to a specificity of 100% for both HMWCK - p63 [fig 11 & fig 12].Out of 4 benign glands only 2 showed positivity for HMWCK and all the 4 showed positivity for p63 staining . Out of 4 premalignant lesion treated with HMWCK and p63, 3 showed positivity for both HMWCK and p3 and 1 showed negativity forboth.[figures1,2,3,4,5,6,7,8,9,10,11,12] The results of our study demonstrates that p63 like HMW-CK is specific for basal cells in the prostate gland and therefore are negative in the areas of prostatic carcinoma. After statistical analysis p63 is found to be more sensitive than HMWCK in staining benign basal cells in TURP specimen.

Table 1-The Result Of Following Cases After Being Treated With Hmwck And P63 Immunostaining

SL. NO.	PATH NO.	HPE	HMWCK(+VE/-VE)	P63(+VE/-VE)
1	3902/10	BPH(Basal cell hyperplasia)	Positive	Positive
2	889/11	BPH(Cystic atrophy)	Positive	Positive
3	530/12	BPH(Crush artifact)	Negative	Positive
4	2413/12	BPH	Negative	Positive
5	4101/12	HGPIN	Positive	Positive

6	3954/11	HGPIN	Positive	Positive
7	3209A/11	HGPIN	Negative	Negative
8	3385/11	HGPIN	Positive	Positive
9	3615/11	Prostatic adenocarcinoma	Negative	Negative
10	704/12	Prostatic adenocarcinoma	Negative	Negative
11	812/12	Prostatic adenocarcinoma	Negative	Negative
12	1185/11	Prostatic adenocarcinoma	Negative	Negative

Table 2 Results Of Hmw-Ck Staining In Benign, Premalignant And Malignant Prostatic Glands

Results Of Hmwck Staining	Benign	Premalignant	Malignant	Total
Positive	2	3	0	5
Negative	2	1	4	7
Total	4	4	4	12

Sensitivity of HMW-CK = 62.5%
Specificity of HMWCK = 100%
Positive predictive value=100%

Statistical inference
$X^2 = 4.800$, d.f. = 2 & p = .091
p = .091 < .05

Table 3 Result Of P63 Staining In Benign, Premalignant And Malignant Prostatic Glands

Results Of P63 Staining	Benign	Premalignant	Malignant	Total
Positive	4	3	0	7
Negative	0	1	4	5
Total	4	4	4	12

Sensitivity of p63 = 87.5%
Specificity of p63 = 100%
Positive predictive value of p63 = 100%

Statistical inference
$X^2 = 8.914$, d.f. = 2 & p = .012
p = .012 < .05

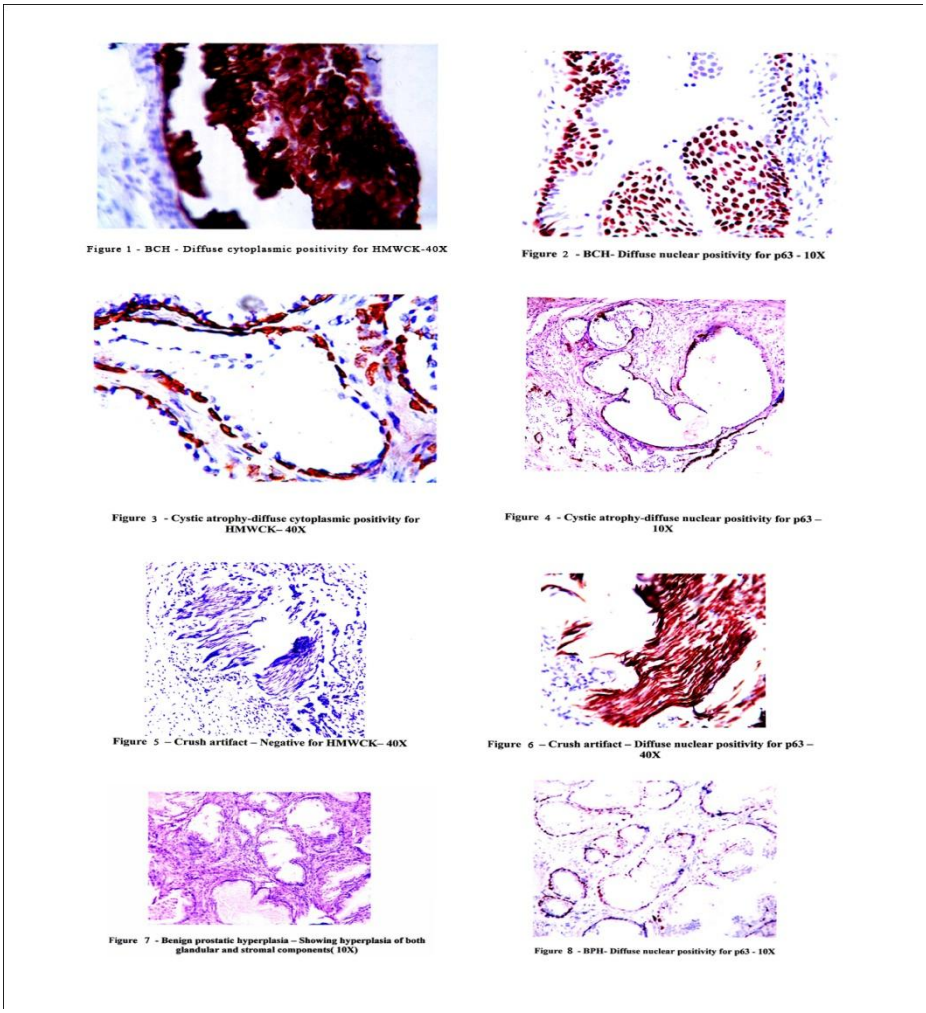

Figure 1 - BCH - Diffuse cytoplasmic positivity for HMWCK-40X

Figure 2 - BCH- Diffuse nuclear positivity for p63 - 10X

Figure 3 - Cystic atrophy-diffuse cytoplasmic positivity for HMWCK– 40X

Figure 4 - Cystic atrophy-diffuse nuclear positivity for p63 – 10X

Figure 5 – Crush artifact – Negative for HMWCK– 40X

Figure 6 – Crush artifact – Diffuse nuclear positivity for p63 – 40X

Figure 7 - Benign prostatic hyperplasia – Showing hyperplasia of both glandular and stromal components(10X)

Figure 8 - BPH- Diffuse nuclear positivity for p63 - 10X

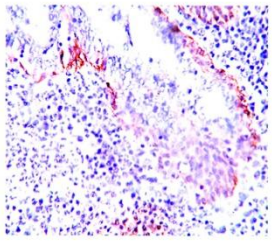

Figure 9 - High grade prostatic intraepithelial neoplasia – Patchy cytoplasmic positivity for HMWCK – 10X

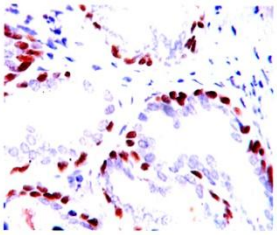

Figure 10 - High grade prostatic intraepithelial neoplasia – Patchy nuclear positivity for p63 – 40X

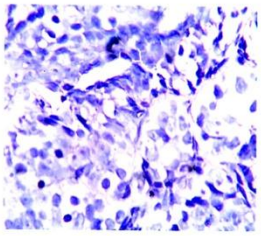

Figure 11 - Adenocarcinoma – Negative for HMWCK – 40X

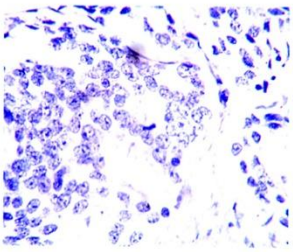

Figure 12 - Adenocarcinoma – Negative for p63 – 40X

1V. Discussion

Prostatism is a common malady in the geriatric age group. Though the diagnosis of the prostatic lesions are analysed through histopathological examination, sometimes, diagnosis can be challenging, when pathologist are faced with certain problems such as small foci of Ca or benign mimickers. In such situation, Immunohistochemical detection of basal cells are widely used. The most commonly used basal cell specific markers are high molecular weight cytokeratin [HMWCK] and newly described basal cell marker p63, HMWCK shows cytoplasmic positivity whereas p63 shows nuclear positivity. Signorette etal [6] also highlighted the role of p63 in the development of prostate gland and showed that p63 is expressed in virtually all the basal cells of prostatic glands including a subset negative for HMW-CK. The results of our study demonstrates that p63, like HMWCK is specific for basal cells in the prostate gland.

None of the 4 case with histologically unequivocal prostatic carcinoma demonstrated immunoreactivity for either HMWCK or p63 [100% specificity. Among the 8 cases which included both benign and premalignant lesions, with regard to HMWCK staining in our study in 5 cases [2 Benign and 3 Premalignant [PIN]] showed positivity, 3 cases [2 Benign and 1 premalignant] showed negativity. Absence of basal cell staining in these cases was due to the effects of prolonged formalin fixation, as extended formalin fixation decreases the HMWCK antigenicity[7] With regard to p63 staining in our study out of 8 cases, 7 cases [4 benign and 3 premalignant [PIN]] showed positivity and 1 case [1 premalignant] showed negativity. This correlated with the study of shah etal [8] who reported the absence of basal cell staining both with HMWCK and p63. This absence of basal cell staining may be attributed to the diminished or absence gene expression of basal cell markers, technical variables, including those resulting from surgical procedures and antigen retrieval methods could be another important source of negative basal cell IHC reaction. Multhaupt etal [9] also found that 88% benign gland in the transition zone obtained by trans urethral resections of the prostate lost their HMWCK antigenicity if antigen retrieval was not used.

In our study, one case of benign prostatic hyperplasia with crush artifact, showed, lack of staining of basal cells with HMWCK but showed positivity with nuclear p63 staining. This correlated with the study of Michael et al [10] who showed same effect as above. In one case of prostatic adenocarcinoma good positive internal control staining was seen with p63. That means, no staining was seen in malignant glands but the basal cells in benign glands that was present adjacent to the malignant gland were stained with p63.

Our study showed that the sensitivity in identifying basal cells in benign glands is 62.5% and 7.5% for HMWCK and p63, respectively. Hence, p63 is slightly more sensitive in identifying basal cells than HMWCK according to our study. Shah et al similarly found that p63 is more sensitive than HMWCK in identifying the basal cells, particularly in TURP specimens, offering slight advantage over HMWCK in diagnostically challenging cases. p63 may be used as an alternative to HMWCK stain for difficult prostatic lesion.

V. Conclusion

In this retrospective study of 150 cases of prostatic lesions, histopathological analysis and the role of IHC markers were studied. It was found that immunohistochemical p63 staining is diagnostically reliable in identifying basal cells in TURP specimens and compares favourably with HMWCK staining. In TURP specimens, in which cautery artifact can impair the ability to detect HMWCK, staining for p63 appears superior. In addition, p63 staining which shows a nuclear reaction is easy to interpret than HMWCK which shows cytoplasmic reaction.

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