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ROLE OF IMMUNOHISTOCHEMISTRY IN EVALUATION OF VARIOUS HISTOPATHOLOGIC MIMICKERS OF PROSTATE ADENOCARCINOMA

Pathology

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ABSTRACT

INTRODUCTION: Prostate cancer is the most common cancer in men and responsible for 10% of all cancer deaths. Its incidence has been increasing because of increase in aging population and as a result of screening techniques like PSA (prostate specific antigen), Digital rectal examination and Ultrasonography. Diagnosis is established by doing TRUS (Transrectal Ultrasound) guided needle prostate biopsy in suspected cases. Tissue diagnosis often becomes difficult because of smaller biopsy samples or due to histopathologic mimickers of prostatic malignancy. These include chronic prostatitis, basal cell hyperplasia, clear cell hyperplasia, atypical adenomatous hyperplasia and sclerosing adenosis. These benign mimickers can lead to serious clinical, psychological and medicolegal consequences. Immunohistochemical markers are often used in these circumstances to rule out malignancy. Basal cell markers are most commonly used for Immunohistochemical evaluation of prostate. Basal cell markers are of 2 types; nuclear marker (p63 and cytokeratin {CK5/6}) and cytoplasmic marker (high molecular weight cytokertin 34Eb12). The lack of basal cell Layer staining along with simultaneous demonstration of a positive basal cell layer in adjacent unequivocally benign glands is the most important diagnostic hallmark of prostatic adenocarcinoma.

AIM & OBJECTIVES: Study different patterns of benign mimickers of prostate adenocarcinoma. Couple it with use of immunohistochemistry(IHC) for accurate diagnosis and avoid false positive interpretation.

MATERIAL AND METHODS: From Dec 2013 to Dec 2017, a prospective study was carried out in the department of pathology, SCB medical College, Cuttack. TRUS guided prostate biopsy samples were collected from 193 cases. A detailed histopathologic and immunohistochemical analysis was then carried out.

RESULTS: Routine Hemotoxylin -Eosin (H/E) stained sections showed BPH in the majority 92(47.67%), followed by suspicious of carcinoma in 32(16.6%) and overt carcinoma in 69(35.7%) cases respectively. Immunohistochemical analysis was done in suspected cases of adenocarcinoma using p63 and 34bE12. Results of IHC were prostate adenocarcinoma (n=8), chronic prostatitis (n= 11), basal cell hyperplasia (n=6), clear cell hyperplasia (n=3) and sclerosing adenosis(n=4)

CONCLUSION: Our study confirms the diagnostic utility of basal cell markers p63 and 34bE12 in differentiating benign mimickers from the malignant ones in morphologically suspicious cases of prostatic biopsy specimens.

KEYWORDS

INTRODUCTION

Prostate cancer is the most common cancer in men and responsible for 10% of all cancer deaths[1]. Its incidence has been increasing because of increase in aging population and as a result of screening techniques like PSA (prostate specific antigen), Digital rectal examination and Ultrasonography[2]. Early diagnosis of prostate cancer carries good prognosis[3]. It is diagnosed by digital rectal examination (DRE), PSA (prostate specific antigen) testing and biopsy[4]. Biopsy samples are often collected from Transrectal Ultrasound (TRUS) guided needle biopsy or resected specimens (TURP chips).

Sometimes, tissue diagnosis becomes difficult because of smaller size of biopsy sample, small focus of cancer or due to presence of benign mimickers of malignancy[5]. These benign mimickers (basal cell hyperplasia, clear cell hyperplasia, atypical adenomatous hyperplasia, chronic prostatitis, prostatic atrophy, normal seminal vesicle or colonic mucosa) can cause serious clinical, psychological and medico legal consequences[6]. Zhou M et al reported that incidence of these benign mimickers ranges from 16 to 20%[7].

Immunohistochemical (IHC) markers are often used as diagnostic tool, especially in the setting of suspected prostatic adenocarcinoma. Loss of basal cells is the most important diagnostic hallmark of malignancy. IHC staining using basal cell layer markers are the cornerstone of prostate carcinoma diagnosis since last 15 years[8]. Basal cell markers are of 2 types; nuclear marker (p63 and cytokeratin {CK5/6}) and cytoplasmic marker (high molecular weight cytokertin: 34Eb12). Diagnosis of carcinoma is based on negative immune reaction and positive staining confirms presence of benign mimickers.

AIMS AND OBJECTIVES

Evaluate the prevalence of various morphologic patterns of benign mimics of prostatic adenocarcinoma. Second, use of Immunohistochemistry (IHC) in order to avoid false positive carcinoma interpretation for accurate diagnosis.

MATERIAL AND METHODS

After obtaining institutional ethical committee approval, a prospective study was carried out in the department of pathology, SCB Medical College; Cuttack from Dec 2016 to Jan 2019. Patients undergoing TRUS guided needle prostate biopsy were included in the study. Open prostate enucleation/TURP (transurethral resection of prostate) chips and radical prostatectomy patients were excluded from study. Clinicopathological parameters (age, PSA level, symptom score, nature of surgical specimens) were analyzed in each case.

Prior to processing, specimens were fixed in 10% formalin. Tissue sections were processed in auto processor for preparation of paraffin blocks. Blocks were kept over ice prior to cutting. These sections were fixed on Mayer's egg albumin to the glass slides. Slides were then stained using Hemotoxylin and Eosin .Nucleus stained blue and cytoplasm stained pink. Benign prostate hyperplasia (BPH) taken as positive control and frank cases of adenocarcinoma were taken as negative control. Histologically suspicious of adenocarcinoma cases were further analyzed by IHC.

Immunohistochemical studies

Evaluation of p63 and 34bE12 were done on paraffin blocks which were chosen for performing IHC. Expression of these two markers was studied in each case. PathnSitu™ ready to use monoclonal antibody (p63-4A4 clone, CKHMW-34bE12) were utilised for this purpose[9]. Diagnosis of carcinoma is based on negative immune reaction and positive staining confirms presence of benign mimickers.

RESULTS

A total of 193 TRUS biopsy samples were analyzed during the study period. All of the cases were subjected to routine clinical examinations, ultrasonography and serum PSA estimations, and then the biopsied samples were studied both macroscopically, microscopically and in suspicious cases, IHC using basal cell markers using p63 and high molecular weight cytokeratin (34bE12) were used to reach the final diagnosis.

Different prostatic lesions found on routine histologic examination are showed in table 1.BPH constitutes the maximum number of cases 92(47.66%) while 32(16.6%) cases were that of mimics and carcinoma constitute 69(35.7%) cases.

Table 1. Distribution of total prostatic samples (n=193)

Pathology	No. of cases (Percentage)
BPH	92(47.7%)
Malignancy	69(35.7%)
Suspicious	32(16.6%)

Table 2 shows correlation of serum PSA with suspicious lesions. Out of 54 cases of suspicious lesions, 13 have normal serum PSA (<4ng/ml), whereas 18 have in gray zone PSA (4-10ng/ml) and only 3 had PSA >10ng/ml.

Table 2. Correlation of serum PSA with suspicious lesions

Serum PSA	Suspicious lesions(n=32)
<4ng/ml	13(40.6%)
4-10ng/ml	10(31.2%)
>10ng/ml	9(28.2%)

Final histological outcome of suspicious lesions based on IHC findings are shown in Table 3. Adenocarcinoma was detected only in 8 cases and rest were various benign mimickers of malignancy. Chronic prostatitis was the most common benign mimicker (n= 11), followed by basal cell hyperplasia (n=6), sclerosing adenosis (n=4) and clear cell hyperplasia (n=3)

Table 3. Histological outcome of suspicious lesions based on IHC findings

Final pathology of suspicious lesions	No. of cases(Percentage)
Chronic prostatitis	11(34.5%)
Basal cell hyperplasia	6(18.7%)
Sclerosing adenosis	4(12.5%)
Clear cell hyperplasia	3(9.3%)
Adenocarcinoma	8(25%)

Sclerosing adenosis on routine H/E staining shows proliferation of glands and stroma mimicking high grade malignancy (Figure 1), but on IHC, positive basal cell cytoplasmic staining (Figure 2) and nuclear staining (Figure 3) rules out adenocarcinoma .

Figure 1. H&E (100X): proliferation of gland and stroma mimicking high grade adenocarcinoma

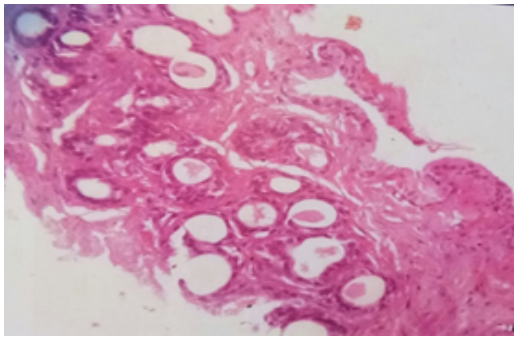

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Figure 2. 34bE12 (100X): Positive basal cell cytoplasmic staining

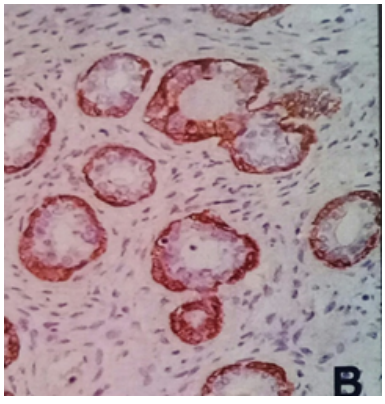
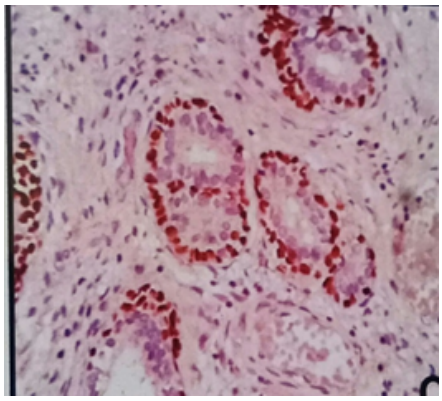


Figure 3. p63 (100X): Positive basal cell nuclear staining



DISCUSSION

We examined 193 core needle prostate biopsy samples over 2 year period. BPH is the most common pathology (52%) which is similar to the study by Angurana et al who studied 200 prostate specimens majority of cases were BPH (50.4%)[10]

There is a direct correlation between serum PSA level and occurrence of prostate adenocarcinoma & inverse relationship with mimickers. Overall incidence of suspicious lesions in our study is 16.6%. There was overlapping of clinical symptoms in most of these cases which is according to a study by Anderson et al who also noted that suspicious lesions do not have specific clinical manifestations[11].

Incidence of benign mimickers like clear cell hyperplasia, sclerosing adenosis, cribiform hyperplasia is similar to those published literature although incidence of chronic prostatitis was higher in our study[12]. Clear cell hyperplasia which accounted for 9.3% cases in our study correlated with Helpap B et al who stated the incidence atypical adenomatous hyperplasia to be 4-15%[13].

Out of 193 core prostatic needle biopsy samples after histopathological analysis using H/E stain, 92(47.7%) cases are confirmed on fibromuscular glandular hyperplasia, 32 (16.6%) cases as mimics of prostate adenocarcinoma, 69 (35.7%) as carcinoma prostate.

Diagnosis of 32 cases which could not be resolved using H/E stain was subjected to immunohistochemical analysis. In 8 out of 32 cases, both basal cell markers were negative supporting the diagnosis of mimics of prostate cancer.

We observed no difference in staining pattern between nuclear and cytoplasmic marker. Shah, Rajal B et al 2002 observed that 34bE12 and P63 are highly specific for basal cells and P63 is more sensitive than 34bE12 in staining benign basal cells[14]. According to that study, p63 offers slight advantage over 34bE12 in diagnostically challenging cases. This may be due to different manufacturers of the antibody and methods of antigen retrieval during immunohistochemical staining[15].

CONCLUSION

The study provides awareness about presence of various benign mimickers which may stimulate carcinoma. Histology of these mimickers are diverse and may range from different histoanatomy, inflammatory, pathophysiologic process

Hence these mimics are often perplexing yet proper observation of their morphological patterns coupled with prudent use of IHC can lead to correct diagnosis & benefit a patient on the long run.

REFERENCES

1. Rawla P. Epidemiology of Prostate Cancer. World J Oncol. 2019 Apr;10(2):63-89
2. WeinerAB, MatulewiczRS, EggenerSE, SchaefferEM. Increasing incidence of metastatic prostate cancer in the United States (2004-2013) Prostate Cancer Prostatic Dis. 2016 Dec;19(4):395-397
3. Kappen S, Jürgens V, Freitag MH, Winter A. Early detection of prostate cancer using prostate-specific antigen testing: an empirical evaluation among general practitioners and urologists. Cancer Manag Res. 2019 Apr 16;11:3079-3097
4. Descotes JL. Diagnosis of prostate cancer. Asian J Urol. 2019 Apr;6(2):129-136.
5. Chen S, Patil PA, Lepe M, Lombardo KA, Amin A, Matoso A. Retrospective Analysis of Atypical Glands Suspicious for Carcinoma in Transurethral Resection of Prostate. Appl Immunohistochem Mol Morphol. 2018 Mar;26(3):186-191
6. Billis A.Prostatic atrophy. Clinicopathological significance. Int Braz J Urol. 2010 Jul-Aug;36(4):401-9.

7. Herawi M, Parwani AV, Irie J, Epstein JI. Small glandular proliferations on needle biopsies: most common benign mimickers of prostatic adenocarcinoma sent in for expert second opinion. Am J Surg Pathol. 2005 Jul;29(7):874-80
8. Xiao X, Hu R, Deng FM, Shen SS, Yang XJ, Wu CL. Practical Applications of Immunohistochemistry in the Diagnosis of Genitourinary Tumors. Arch Pathol Lab Med. 2017 Sep;141(9):1181-1194
9. PathnSituBiotechnologies. http://pathnsitu.com/subproducts.php?cat=3(accessed on 24 Feb 2019)
10. Neha Angurana. Pattern of Prostate diseases. A histopathologic study in Jammu. Journal of Basic and Applied Medical Sciences2014 Vol. 4 (3) September-December, pp. 163-16
11. Anderson's pathology. Edited by Ivan Damjonov &James Linder, 10th edition, 1996(Mosby) pp 2166-2230
12. Yuqiao Xu,Yingmei Wang,Ru Zhou,Haiyang Li, Hong Cheng. The benign mimickers of prostatic acinar adenocarcinomaChin J Cancer Res. 2016 Feb; 28(1): 72–79
13. Helpap B: Observation on the number, size and localization of neucleoli in hyperplastic and neoplastic prostatic disease. Histopathology 13:203,198
14. Shah, Rajal B, Zhou, Ming .Prostate biopsy interpretation. An illustrated guide. 2012. Springer
15. Monoclonal Antibody Production. National Research Council (US) Committee on Methods of Producing Monoclonal Antibodies. Washington (DC): National Academies Press (US); 1999