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RESEARCH ARTICLE

HISTOPATHOLOGICAL SPECTRUM OF NON-NEOPLASTIC AND NEOPLASTIC PROSTATE LESIONS AND ITS ASSOCIATION WITH HIGH MOLECULAR WEIGHT CYTOKERATIN (HMWCK)

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ABSTRACT

Of the diseases which affects the prostate the most frequently encountered lesions in clinical practice are benign prostatic hyperplasia, prostatitis and prostatic cancer (Cotran *et al.,* 1994). Proliferative activity and invasiveness of prostatic glands increases from the benign to malignant end in the spectrum of prostatic lesions. For histopathological diagnosis, H&E (Hematoxylin and Eosin) staining is the gold standard. But sometimes on routine H&E staining prostatic lesions cause a diagnostic dilemma. In addition to routine staining, immunohistochemistry markers such as HMWCK play an important role in suspicious cases. The main aim of our study is to study the histopathological spectrum of prostatic biopsies and use of immunohistochemistry in addition to H & E staining in suspicious cases. This study was conducted in the Department of Pathology, AIMSR Bathinda, India on 146 biopsies. In our study 26.86% cases were neoplastic and 73.16% were non-neoplastic. The most common pattern seenin neoplastic lesions were ill defined glands and fused microacinar pattern. IHC was done on 60 suspicious cases. In 10 cases the diagnosis was changed on the basis of IHC marker (HMWCK). In 8 cases the diagnosis was changed from non- neoplastic to neoplastic whereas in 2 cases from neoplastic to non-neoplastic. From our study, we came to the conclusion that HMWCK marker should be strongly recommended in all suspicious areas in prostatic biopsies to remove any subjective error by a pathologist.

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INTRODUCTION

The prostate gland is a retroperitoneal organ encircling the neck of the urinary bladder and urethra and is devoid of distinct capsule and weighs approximately 20 grams. Histologically the prostate is composed of glands lined by two layers of cells: a basal layer of low cuboidal epithelium covered by a layer of columnar secretory cells. These glands are separated by abundant fibromuscular stroma. Enlargement or growth of prostate due to nodular hyperplasia or prostatic intraepithelial neoplasia or adenocarcinoma may give rise to bladder outlet obstruction (Kantikundo *et al.,* 2014). Benign prostatic hyperplasia is an extremely common condition in men over the age of 50 yearsfollowed by prostatitis and carcinoma prostate (Walsh, 1986).Benign prostatic hyperplasia (BPH) is the usual name applied to a common benign disorder of the prostate that, when extensive, results in varying degrees of urinary obstruction.

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The disease represents a nodular enlargement of the gland caused by hyperplasia of both glandular and stromal components.The clinical incidence of this disease is only 8% during the fourth decade, but it reaches 50% in the fifth decade and 75% in the eighth decade. It has been estimated that the process begins before the age of 30 and that its doubling time progressively increases from 4.3 years in the early stage (third to fifth decade) to over 100 years in the late stage (patients beyond 70 years old) (Berry *et al.,* 1984). In only about 5% cases, will a focal lesion of nodular hyperplasia be found in the peripheral zone of the organ (Kerley *et al.,* 1997; Ohori *et al.,* 1994; Oyen *et al.,* 1993). Prostate cancer is the leading cause of cancer in men and is second only to lung cancer as a leading cause of cancer related deaths in men. Rate among black males are one and a half than those of white males (Bostwick *et al.,* 2004). There is no convincing evidence that patients with nodular hyperplasia are at increased risk for development of prostatic carcinoma, although the two conditions often co-exist (Bostwick *et al.,* 1992; Hammarsten *et al.,* 1994; Kearse *et al.,* 1993). Biopsy and histopathology remains the gold standard for final diagnosis of prostate cancer. Histopathological

diagnosis of prostatic cancer is usually based on morphological features such as pattern of growth, atypical features seen in nucleus and presence or absence of basal cells. These days application of immunohistochemistry plays an important role in challenging cases particularly with mixture of both malignant and benign tissue. Several new markers are now used including basal cell marker high-molecular-weight-cytokeratin (HMWCK, clone 34βE12) and the prostate biomar ker alpha-methylacyl-CoA-racemase (AMACR) (Trpkov *et al.,* 2009).

Advantages of using immunohistochemistry (IHC) over routine H & E stain

- The use of HMWCK antibody to mark basal cell is currently a common practice in order to avoid re-biopsies.
- Prostatic lesions on routine staining sometimes cause a diagnostic dilemma, especially when the malignant tissue is limited and is mixed with benign prostatic glands or because of the presence of benign mimickers of carcinoma. The application of Immunohistochemistry contributes a valuable differential diagnosis.

Two important serum markers for prostatic epithelium demonstrable in routinely processed material with polyclonal or monoclonal antibody are PAP (prostatic acid phosphatise) and PSA (prostate specific antigen) (Shevchuk *et al.,* 1983; Stein *et al.,* 1982; Papsidero *et al.,* 1985). PSA is a glycoprotein that has been identified as a kallikrein-like protease (Allsbrook and Simms, 2005). It is a product of prostatic epithelium. PSA is organ specific not cancer specific. Its normal value is 0-4ng/ml. However, this cut off between normal and abnormal may be too high because 20% to 40% of patients with organ confined prostate cancer have a PSA value of 4ng/ml or less. Thus, some guidelines consider PSA values above 2.5ng/ml abnormal.

MATERIALS AND METHODS

The study was conducted in the Department of Pathology in Adesh Institute of Medical Sciences And Research, Bathinda on all the specimens collected over a period of 6.5 years (i.e. 5.5years retrospective from 1st Jan 2010 to 30th June 2015 and 1 yr prospective from 1st July 2015 to 30th June 2016). A total of 146cases were studied and reviewed by two histopathologists for final diagnosis.

The cases were then subjected to following study:

A. Clinical study:

a) For every patient included, data was recorded on proforma which included patients name, identification number, sex, and age and histopathology number.
b) Detailed history including duration of incontinence of urine, frequency of micturation and urgency was noted.
c) Relevant investigations like PSA levels if done were noted.

B. Gross study: Specimens were studied in detailfor gross morphology and adequate number of sections was taken.

C. Microscopic Examination: A careful histopathological examination was carried out on all tissues. The sections were processed by first fixing in 10% formalin followed by automatic tissue processing, paraffin embedding, sectioncutting and staining. Hematoxylin and eosin was the routine stain.

D. Immunohistochemical studies: Immunohistochemical Proc edure. The Avidin Biotin Complex (ABC) detection system was used on specimen of formalin fixed, paraffin embedded tissue sections. Tumor marker used was High Molecular Weight Cytokeratin (HMWCK).

RESULTS

Out of 146 cases studied, neoplastic lesions were seen in 38 cases i.e. prevalence of prostatic carcinoma in our study was 26.38% and non- neoplastic lesions were seen in 106 cases (72.60%). Table I and II shows that maximum cases of both neoplastic and non- neoplastic lesions were in the age group 61-70 years and very less no. of cases are in the lower age group i.e. <50years. Table 3 shows that majority of the patients 79.1% had complaints of frequency of micturition, while 47.22% of patients had nocturia, 20.8% had hesitancy and 16.6% had urinary retention. The most common presentation was frequency of micturition.

Table 1. Age distribution in Neoplastic Cases

Age (in years)	No of patients (Neoplastic)	Percentage (%)
<50	4	10.52
51-60	10	26.31
61-70	16	42.10
71-80	4	10.52
81-90	2	5.26
>90	1	5.26
Total	38	100

Table 2. Age distribution in Non-Neoplastic Cases

Age (in years)	No of patients (Non neoplastic)	Percentage (%)
<50	4	3.77
51-60	26	24.52
61-70	40	37.73
71-80	32	30.18
81-90	2	1.88
>90	2	1.88
Total	106	100

All prostatic carcinoma cases show different growth patterns. Out of total 38 cases, the most common pattern seen is ill defined glands in 20 cases (52.63%), followed by fused microglandular pattern in 10 cases (26.31%), cribriform pattern in 4(10.52%), hypernephroid in 2(5.26%) and also comedonecrosis in 2(5.26%).

Table 3. Histopathological patterns of prostate carcinoma

Histopathological features	Total no of cases	Percentage (%)
Ill defined glands	20	52.63
Fused microacinar glands	10	26.31
Cribriform pattern	4	10.52
Hypernephroid pattern	2	5.26
Comedonecrosis	2	5.26
Total	38	100

Table 4. Perineural invasion in neoplastic cases

Perineural invasion	No of cases	Percentage(%)
Present	16	42.10
Absent	22	57.89
Total	38	100

Perineural invasion is seen in 16(42.10%) cases.

HMWCK was used in 60 cases. Out of which it was positive in 20(100%) cases of BPH and negative in 24 (100%) cases of adenocarcinoma. 4 cases of low grade PIN showed HMWCK+ and 6 cases of high grade PIN showed HMWCK-. HMWCK was done on 6cases of BPH with suspicious foci, 2 (33.33%) out of them showed positivity with HMWCK and 4(66.66%) showed negativity.

Table 5. Results after using HMWCK on prostatic specimens

Category	No of cases	HMWCK +ve	HMWCK-ve
BPH	20	20	
Adenocarcinoma	24		24
PIN low grade	4	4	
PIN high grade	6		6
BPH with suspicious foci	6	2	4
Total	60	26	34

Out of total 144 cases, 106(73.61%) were non-neoplastic and 38(26.38%) were neoplastic on HPE. After using HMWCK 96(66.66%) came out to be non-neoplastic and 48(33.33%) were neoplastic.

Table 6. Final diagnosis after using IHC (HMWCK) marker

Lesion	Before HMWCK	After HMWCK
Non-neoplastic	106	96
Neoplastic	38	48
Total	144	144

Table 7. Out of 10 cases in which the diagnosis is changed, 2 belongs to age group 41-50years, and 8 belongs to age group 51-60 years

Age group (in years)	No of cases	Diagnosis on HPE	Final Diagnosis considering HPE and IHC
41-50	2	Non-neoplastic	Neoplastic
51-60	8	Non-neoplastic	Neoplastic

DISCUSSION

Age distribution

Maximum no of patients belong to age group 61-70 years with 16 patients (42.10%) in neoplastic cases and 40 patients (37.73%) in non-neoplastic cases. Mean age of the patients was 65.76years. The minimum age was 45 years while the maximum was 92 years. No significant difference was noted in the mean age of the nonneoplastic and neoplastic groups. The results of the present study agree with the studies by George and Thomas, (2005) in 2004 who also found maximum no of patients in age group 61-70 years and mean age was 66.81 years, and by Barakzai *et al* (2011) in 2011in which the mean age was 66.9 years. Garg *et al* (2013) in 2013 also show similar results with maximum no of patients in age group 61-70 years and mean age was 68.6 years. The decline in the number of cases beyond the age of 80 years reflects the average life span of people in our country.

Histopathological spectrum in prostatic cancinoma

All prostate carcinoma cases show different growth patterns. Out of total 38 cases, the most common pattern was ill defined glands seen in 20 cases (52.63%), followed by fused microglandular pattern in 10(26.31%), cribriform pattern in 4(10.52%), hypernephroid in 2(5.26%) and comedonecrosis in 2 cases(5.26%). More or less similar results were found in the study by Gottipatti *et al* (2015) in 2012and Garg *et al* (2013) in 2013. Perneural invasion was seen in 16 cases (42.10%) which is corresponding to a study done by Bastacky et al in 1993 who stated that 20% cases were showing perineural invasion and Garg et al in 2013 who observed that 42.5% cases were showing perineural invasion. Similar results were found in a study of Garg *et al* in 2013 which observed on hematoxylin and eosinstaining shows 20 cases were non-neoplastic and 22 were neoplastic while after applying HMWCK, 21 came out to be non-neoplastic and 24 came out to be neoplastic.

Conclusion

Proliferative activity and invasiveness increases from benign to malignant end in the spectrum of prostatic lesions. Histopathology remains the gold standard. However, as an adjunct to routine hematoxylin and eosin (H&E) stain, proliferative markers and basal cell markers have value for resolving suspicious or atypical cases. IHC plays an important role in the diagnosis of prostatic lesions and helps to differentiate malignant glands from benign lesions, especially for lesions in the grey zone in routine histopathological study.

Conflict Of Interest

There is no conflict of interest.

REFERENCES

Allsbrook Jr WC, and Simms, WW. 1992. Histochemistry of the prostate. *Hum Pathol*., 23:297-305.

Barakzai, MA., Mubarak, M. and Kazi, JI. 2011. Histopathological lesions in transrectal ultrasound guided biopsies of prostate in patients with raised serum prostate specific antigen: a preliminary report. *Nephro-Urol Mon*., 3:186–90.

Bastacky, SI., Walsh, PC. and Epstein, JI. 1993. Relationship between perineuraltumor invasion on needle biopsy and radical prostatectomy capsular penetration in clinical stage B adenocarcinoma of the prostate. *Am J SurgPathol.,* 17:336–41.

Berry, SJ., Coffey, DS., Walsh, PC. and Ewing, LL. 1984. The development of human benign prostatic hyperplasia with age. *J Urol.,*132:474-479.

Bostwick, DG. Cooner, H. Denis, L. Jones, GW. Scardino, PT. and Murphy, GP. 1992. Then association of benign prostatic hyperplasia and cancer of the prostate. *Cancer,* 70 (Suppl 1):291-301.

Bostwick, DG., Burke, HB., Djakiew, D., Euling, S., Ho, SM., Landolph, J., Morrison, H., Sonawane, B., Shifflett T, Wate rs, DJ. and Timms, B. 2004. Human prostate cancer risk factors. *Cancer*, 101:2371-2490.

Cotran, RS., Kumar, V. and Robbins, SI. 1994. Prostate. In: Cotran RS, Kumar V, Robbins SI (eds): Robbins Pathologic Basis Of Disease, 6th ed., Philadelphia: *Saunders Co*., pp. 1025-1034.

Garg, M., Kaur, G., Malhotra, V. and Garg, R. 2013. Histopathological spectrum of 364 prostatic specimens including immunohistochemistry wuth special reference to grey zone lesion. *Prostate Int*., 1(4):146-151.

George, E. and Thomas, S. 2005. A histopathologic survey of prostate disease in the sultanate of oman. *Internet J Pathol.,*3(2).

Gottipati, S., Warncke, J., Vollma, R. and Humphrey, PA. 2015. Usual and unusual histologic pattern of high Gleason

score 8 to 10 adenocarcinoma of the prostate in needle biopsy tissue. *Am J Surg Pathol.,* Jun; 36(6):900-907.

Hammarsten, J., Andersson, S., Holmen, A., Hogstedt, B. and Peeker, R. 1994. Does transurethral resection of a clinically benign prostate gland increase the risk of developing clinical prostate cancer? A 10-year follow-up study. *Cancer*, 74:2347-2351.

Kantikundo, SNS., Bhattacharyya, NK., Bhattacharyya, PK. and Kundu, AK. 2014. Astudy to correlate histopathology, biochemical marker and immunohistochemical expression of sex-steroid receptor in prostatic growth. *Indian J Med PaediatrOncol*, jan-mar;35(1): 40- 43.

Kearse Jr WS, Seay TM, Thompson IM: The long-term risk of development of prostate cancer in patients with benign prostatic hyperplasia. Correlation with stage A1 disease. J Urol 1993; 150:1746-1748.

Kerley, SW., Corica, FA., Qian, J., Meyers, RP. and Bostwick DG. 1997. Peripheral zone involvement by prostatic hyperplasia. *J UrolPathol*,6:87-94.

Ohori, M., Egawa, S. and Wheeler, TM. 1994. Nodules rese mbling nodular hyperplasia in the peripheral zone of the prostate gland. *J UrolPathol*, 2:223-234.

Oyen, RH., VandeVoorde, WM., VanPoppel, HP., Brys, PP. A meye, FE., Franssens, YM., Baert, AL. and Baert, LV. 1993. Benign hyperplastic nodules that originate in the peripheral zone of the prostate gland. *Radiology*, 189:707-711.

Papsidero, LD., Croghan, GA., Asirwatham, J., Gaeta, J., Aben oza, P., Englander, L. and Valenzuela L. 1985. Immunohistochemical demonstration of prostate-specific antigen in metastases with the use of monoclonal antibody F5. *Am J Pathol*, 121:451-454.

Shevchuk, MM., Romas, NA., Ng, PY., Tannenbaum, M. and Olsson, CA. 1983. Acid phosphatase localization in prostatic carcinoma. A comparison of monoclonal antibody to heteroantisera. *Cancer*, 52:1642-1646.

Stein, BS., Vangore, S., Petersen, RO. And Kendall, AR. 1982. Immunoperoxidase localization of prostate-specific antigen. *Am J SurgPathol,* 6:553-557.

Trpkov, K., Bartczak-McKay, J. and Yilmaz, A. 2009. Usefulness of cytokeratin 5/6 and AMACR applied as double sequential immunostains for diagnostic assessment of problematic prostate specimens. *Am J Clin Pathol.,* 132:211–20.

Walsh, Pc. 1986. Benign prostatic hyperplasia. In: Walsh Pc, Gittes, RF., Perlmatter, AD. And Stamey, TA. (eds): Campbell's Urology 5th ed., vol.2, Philadelphia: *W.B. Saunders co*., pp. 1248-1265.

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