HISTOMORPHOLOGICAL PROFILE OF PROSTATE BIOPSIES AND CORRELATION WITH SERUM TPSA LEVEL

Laishram Deepak Kumar[1], Gurumayum Laxmikanta Sharma[2], Bijoya Debnath[3], Laishram Rajesh Singh[4], Kaushik Debnath[5]

[1]Demonstrator, Department of Pathology, Regional Institute of Medical Sciences, Imphal.
[2]Senior Resident, Department of Pathology, Regional Institute of Medical Sciences, Imphal.
[3]Trainee, Department of Pathology, Shri Balaji Medical College, Chennai.
[4]Associate Professor, Department of Pathology, Regional Institute of Medical Sciences, Imphal.
[5]Professor, Department of Pathology, Regional Institute of Medical Sciences, Imphal.

ABSTRACT

BACKGROUND

In our study, 50 cases of transurethral prostate biopsies were evaluated histopathologically in the Department of Pathology in collaboration with Department of Urology, Regional Institute of Medical Sciences, Imphal, from October 2013 to September 2015. Total PSA (tPSA) was estimated from serum samples in all cases.

MATERIALS AND METHODS

A total of 50 patients with elevated serum tPSA levels were inducted in this study and prostate needle biopsies taken. Matched prostatectomy specimens were also obtained for 7 cases. Specimens were kept in 10% formalin saline, grossing done and tissues processed. H and E stained sections were examined and the different histomorphological features noted. Gleason scoring system was used in cancers to stratify it.

RESULTS

Out of the 50 cases, 30 malignant (all adenocarcinomas), 4 premalignant and 16 benign cases were found. Gleason scoring on needle biopsies were compared against the prostatectomy specimens. In 5 carcinoma cases with Gleason score 3+3=6 on needle biopsy, 4 cases had similar findings in the corresponding prostatectomy specimens, however, it was upgraded in 1 case. Intermediate differentiation prostatic carcinomas with Gleason score 3+4=7 in needle biopsies were comparable with prostatectomy specimens in 2 cases. The differentiation of prostatic carcinoma vis-a-vis Gleason scoring correlated well with the PSA values. In carcinomas, tPSA value and the Gleason score had a very good correlation (r_s = 0.908). Mean PSA value was found to increase from benign to premalignant and malignant cases, this was found to be statistically significant ($p<0.05$).

CONCLUSION

Use of newer technologies like MRI and serum PSA as a screening tool for prostate pathology have made it possible to identify prostate cancer at an earlier stage in younger age group and has an increased case detection rate. However, there is no marker to predict disease course and at times lead to overtreatment. Image-guided prostate biopsy has a good patient compliance and is advantageous for procurement of representative material. While literatures have claimed that MRI can distinguish benign from malignant lesions accurately, the age old 'histopathology' still remains the gold standard.

KEYWORDS

Transurethral Prostate Biopsies, Prostatectomy Specimens, Total PSA, Gleason Scoring.

HOW TO CITE THIS ARTICLE: Kumar LD, Sharma GL, Debnath B, et al. Histomorphological profile of prostate biopsies and correlation with serum tPSA level. J. Evid. Based Med. Healthc. 2017; 4(88), 5181-5187. DOI: 10.18410/jebmh/2017/1035

BACKGROUND

The prostate gland in an adult man without hyperplasia weighs about 30-40 g lies anterior to the rectum with the urethra running through its center making it amenable to transrectal needle biopsy and transurethral resection.

Financial or Other, Competing Interest: None.
Submission 21-10-2017, Peer Review 28-10-2017,
Acceptance 02-11-2017, Published 04-11-2017.
Corresponding Author:
Dr. Laishram Deepak Kumar,
Demonstrator, Department of Pathology,
RIMS, Lamphelpat, Imphal West - 795004.
E-mail: ldeepakdr@gmail.com
DOI: 10.18410/jebmh/2017/1035

Different prostatic diseases have predilection for a particular zone. Atrophy of the gland is most frequent in the peripheral zone, Benign Prostatic Hyperplasia (BPH) in the transition zone, inflammation in the central zone and carcinoma in the peripheral zone (70%).[1]

Procurement of tissue by transrectal needle biopsy gives a good tissue yield for both the peripheral and central zones, but has a poor yield for the transition zone, whereas the reverse is true for tissue sampling by transurethral resection.[2]

Individual glands of the prostate are medium to large in size and forms lobulated architecture with intervening fibromuscular stroma. The inner side of the gland has papillary infoldings of the lining epithelium, which consist of two major cell types - secretory and basal cells. There are

also several other cell types intermediate between these two types called basal intermediate and secretory intermediate, the existence of which can be proven immunohistochemically. Secretory cells are terminally differentiated cells and are positive for immunohistochemical markers like Total Prostate Specific Antigen (tPSA), Prostate-Specific Acid Phosphatase (PAP) and Prostate-Specific Membrane Antigen (PSMA). Basal cells are stem cells and are negative for the above markers, but positive for high molecular weight cytokeratin like 34ßE12 or cytokeratin 5/6 and low molecular weight cytokeratins like 14 and p63. Basal cell intermediate are negative for cytokeratin 14 and secretory intermediate are positive for cytokeratin 5, which is negative in terminally differentiated secretory cell. Morphologically secretory cells situated on the luminal side have reddish granular nuclei with moderate amount of pale to clear cytoplasm, whereas basal cells situated towards the periphery have bluish-gray smooth nuclei with scanty cytoplasm.[3]

The population-based cancer registry under National Cancer Registry Programme of Indian Council of Medical Research (NCRP of ICMR), Regional Institute of Medical Sciences, Imphal, has been functioning under the Department of Pathology, RIMS, since January 2003. The total number of prostate cancers diagnosed between the year 2006 and 2008 was 30 out of 1934 cancers detected among the male population of Manipur. The most vulnerable and the second most vulnerable age groups were that of ≥75 years (14 of 30 cases) and 70 to 74 years (8 of 30 cases) consisting 1.7% and 1.4% of the population, respectively.[4]

TPSA, which is a kallikrein-like serine protease causing liquefaction of the seminal coagulum is synthesised by the epithelial cell of the prostate gland under androgen receptor regulation. It is produced by both non-malignant and malignant epithelial cells, which makes it prostate specific, but not prostate cancer specific. Serum tPSA increase may occur due to prostatitis, BPH and prostate cancer. Epidemiologic studies have shown that the risk of being diagnosed as prostate cancer increases by a factor of 2 if one first-degree relative is affected and by 4 if two or more are affected. Current estimates are that 40% of early onset and 5-10% of all prostate cancers are hereditary. Prostate cancer affects ethnic groups' differently.[5]

Aims and Objectives

Our study was commenced with an aim to study the pattern of lesions in prostate needle biopsy tissue to correlate the histomorphology of the biopsy and prostatectomy specimen and to correlate the serum tPSA level with the different prostatic pathology.

MATERIALS AND METHODS

The study was a hospital-based cross-sectional one carried out in the Department of Pathology in collaboration with the Department of Urology, RIMS, Imphal, for a period of two years (October 2013 to September 2015). Approval from the Institutional Ethics Committee (IEC), RIMS, was taken before starting the study.

Entire prostate biopsy specimens obtained by Ultrasonography (USG) guided transrectal prostate biopsy and all prostatectomy specimens preceded by biopsy study in the Department of Urology, RIMS, were included. Corresponding blood samples were taken for serum tPSA levels. Histopathologically-proven cases of metastatic carcinoma of the prostate, inadequate prostate biopsies and unwilling patients were excluded.

Total of 50 patients with elevated serum tPSA levels who had undergone prostate needle biopsies including 7 matched prostatectomy specimens were inducted in this study.

Histopathology by exploiting Hematoxylin and Eosin (H and E) stain is regarded as gold standard for distinguishing benign and malignant cases. Specimens were kept in 10% formalin saline overnight and grossing was done on the next day. While grossing, the respective zones from where the cores were taken, number of core (s) and their lengths were noted. The tissue pieces were then processed in our Leica automated tissue processor. Sections were obtained and stained with conventional H and E stain examined in detail and histological findings noted. Gleason scoring system was used for any prostate cancer to stratify it.

Estimation of serum tPSA levels by ELISA method was done for all the cases.

IBM SPSS software was used and descriptive statistics, Spearman's Rho correlation and one-way ANOVA test (analysis of variance) were performed to correlate the data and test the degree of significance.

RESULTS AND OBSERVATION

Out of the 50 cases, maximum number of cases were of malignancies, prostatic adenocarcinoma consisting 30 (60%) cases. Premalignant cases namely benign prostatic hyperplasia with high-grade prostatic intraepithelial neoplasia (BPH with HGPIN), normal benign gland with high-grade PIN (NG with HGPIN) and atypical small acinar proliferation (ASAP) constitute 1 (2%), 1 (2%) and 2 (4%), respectively (Table 1).

Age of the patients ranges from 57 to 88 years (mean = 72.5 years). The maximum number of malignant cases were found in the age range 70 to 79 years (mean = 74.5 years) and the minimum number of malignant cases were found in the range 50 to 59 years (mean = 54.5 years). Maximum number of premalignant cases, which include BPH with HGPIN and NG with HGPIN were found is in the range 60 to 69 years (mean = 64.5 years) while that of the distinct premalignant entity. ASAP was found in the range 50 to 59 years (mean = 54.5 years).

The present study utilises modified Gleason grading system as proposed by the International Society of Urologic and Surgical Pathology (ISUP). Out of the 50 cases studied, there were 7 malignant cases where both needle biopsies and prostatectomy specimens could be compared. While attempting to correlate Gleason grading of biopsy and resected specimens, it is found that in one case, there is an

upgradation of score from 3 + 3 = 6 in biopsy to 3 + 4 = 7 in prostatectomy specimen.

While correlating tPSA values with different lesions of the prostate, there is an increasing trend of tPSA values from benign to premalignant and malignant lesions. This was found to have a high statistical significance (p=0.000) using ANOVA test (Table 2).

It is found that the tPSA value and the Gleason score had a very good correlation (r_s=0.908) and is found to be statistically significant (p=0.000) (Figure 2).

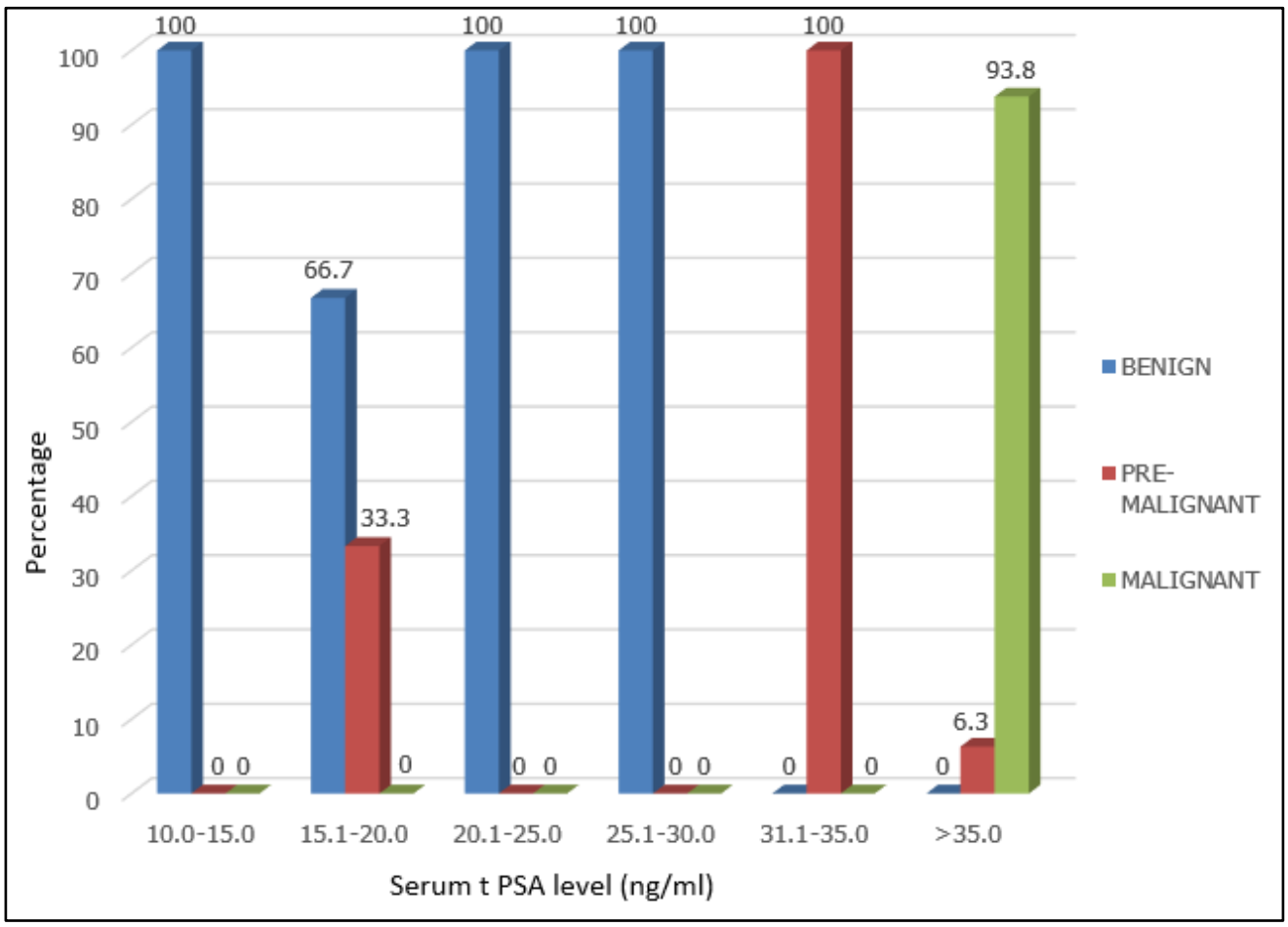

Figure 1. Relation between Serum tPSA and the Types of Neoplasm

Diagnosis	Number (%)
Prostatic Adenocarcinoma (ADC)	30 (60)
Benign Prostatic Hyperplasia (BPH)	5 (10)
Normal Gland (NG)	5 (5)
Benign Prostatic Hyperplasia with Chronic Prostatitis (BPH + CP)	3 (6)
Atypical Small Acinar Proliferation (ASAP)	2 (4)
Benign Prostatic Hyperplasia with High-Grade Prostatic Intraepithelial Neoplasia (BPH + HGPIN)	1 (2)
Benign Prostatic Hyperplasia with Low-Grade Prostatic Intraepithelial Neoplasia (BPH + LGPIN)	1 (2)
Granulomatous Prostatitis (GP)	1 (2)
Normal Gland with High-Grade Prostatic Intraepithelial Neoplasia (NG + HGPIN)	1 (2)
Normal Gland with Low-Grade Prostatic Intraepithelial Neoplasia (NG + LGPIN)	1 (2)
Total	**30 (100)**

Table 1. Different Histological Findings, Number of Cases and their Percentages

Category	Number of Cases	Mean of tPSA (SD)	p-value
Benign	16	18.18 (6.10)	0.000
Premalignant	4	36.42 (14.80)	
Malignant	30	94.13 (30.76)	

Table 2. Significance of the Mean tPSA Levels among the Types of Neoplasm using One-Way ANOVA Test

Features	Number of Cases (%)
Cribriform Gleason grade 4	9 (30)
Perineural invasion	8 (26.6)

HGPIN (High-Grade PIN)	6 (20)
Glomerulation	4 (13.3)
Atrophy	2 (6.7)
Mucinous fibroplasias/collagenous micronodule	1 (3.3)
Eosinophilic crystalloid	1 (3.3)
IDC-P (intraductal carcinoma prostate)	1 (3.3)
Corpora amylacea	1 (3.3)
Cribriform Gleason grade 3	1 (3.3)
Adenocarcinoma with ductal differentiation	1 (3.3)
Total malignant cases	30 (100)

Table 3. Histomorphological Profile of Malignant Lesions (Percentage being Calculated among the 30 Malignant Cases)

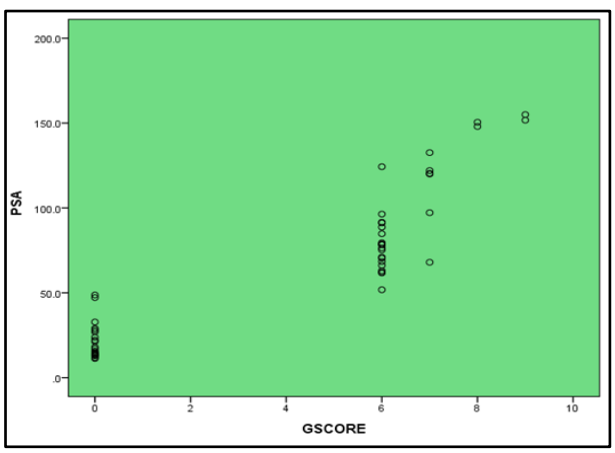

Figure 2. Scatter Diagram Showing Relation between Serum tPSA and Gleason Score (G Score) r_s (Spearman's rho) = 0.908, p-value = 0.000

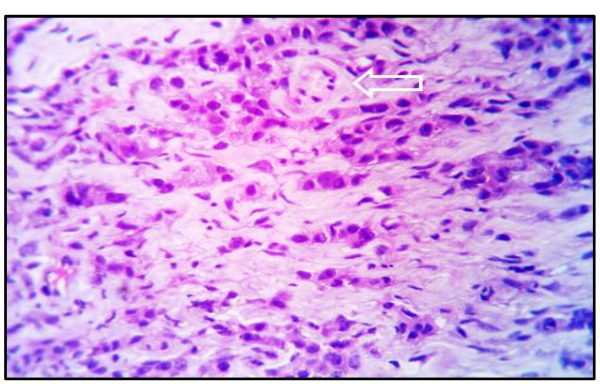

Figure 3. Photomicrograph Showing Perineural Invasion (H and E; 40x)

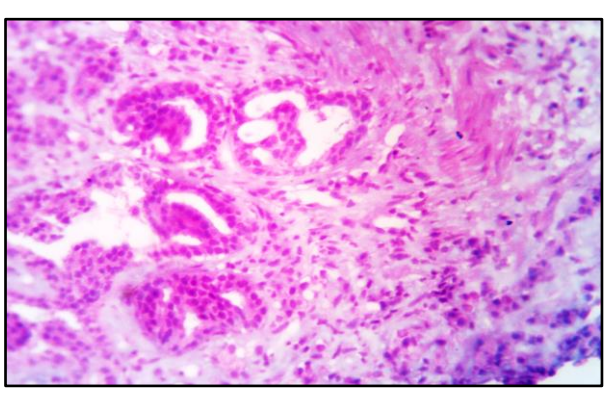

Figure 4. Photomicrograph Showing Malignant Glands Forming Glomeruloid Body (H and E; 40x)

DISCUSSION

With the widespread use of serum tPSA as a screening tool and subsequent biopsy to diagnose prostate carcinoma, the clinicopathological characteristics of prostate carcinoma have changed significantly. The most remarkable one is "stage migration", i.e. the diagnosis of prostate cancers in prostates with a smaller volume and at a younger age. There is also an increase in the incidence of nonpalpable cancers between 1988 and 1996 from 10% to 73%.[6] Although, the worldwide incidence of prostate carcinoma has increased dramatically, many of these patients have clinically insignificant disease. In this study, the incidence of prostate cancer was found in the older age group, i.e. in the range of 70 to 79 years (mean = 74.5 years). The possible explanation maybe our study of only symptomatic cases, small sample size and ignorance of the patients.

In this study, the incidence of mucinous fibroplasia, one of the diagnostic features of prostate carcinoma defined as acellular or hypocellular hyalinised stroma within or outside the cancer glands was 3.3% (Table 3). This finding is similar to that of a study conducted by Thorson P et al[7] who found the incidence of mucinous fibroplasia in biopsies to be 1-2%.

The diagnostic features of prostate cancer other than mucinous fibroplasia are perineural invasion and glomerulation of the cancer glands. Perineural invasion is characterised by tight circumferential or near circumferential encircling of a nerve by a malignant gland and has a reported incidence of 17%, which in our study is 26.6% (Table 3).[8] Glomerulation characterised by balls or tufts of cancer cells within a cancer gland, superficially resembling a glomerulus has a reported incidence of 3-15%,[9] which in our study is 13.3% (Table 3).

Prostatic Intraepithelial Neoplasia (PIN) considered to be a precursor lesion in prostate carcinoma is characterised by secretory epithelial proliferation within the prostate gland and acini that display significant cytologic atypia. Based on the degree of atypia, it can be categorised into low-grade PIN (LGPIN) and high-grade PIN (HGPIN). LGPIN is not associated with increased cancer detection in subsequent followup biopsies and is usually not reported. HGPIN diagnosed on needle biopsies carries 22-25% risk of finding cancer in subsequent biopsies. Incidence rate of HGPIN on needle biopsies ranges from 0-24% (mean = 7.7%, median = 5.2%).[10] In our study, the incidence of HGPIN and LGPIN in benign cases were 4% each and that in malignant cases was 20% (Table 3). The recommended time of a repeat

biopsy study after the diagnosis of HGPIN on biopsy is within 1-3 years or within 12 months if the initial biopsy was a six core sextant biopsy.[11]

ASAP is a small focus of prostate glands that exhibit some architectural and cytological atypia and is suspicious for, yet falls short of the diagnostic threshold for prostate cancer. The important factors that result in the diagnosis of ASAP are minimally sampled tissue in needle biopsy, crush artefact, poorly-stained tissue sections, atypical glands at the tip or edge of a biopsy core, inherent difficulty to differentiate between cancer and adenosis and between cancer and partial atrophy, etc. The diagnosis of ASAP has a significant risk for detecting prostate cancer in subsequent biopsies ranging from 17-70% (average of 42%) in published studies. Patients with ASAP are therefore recommended to undergo immediate repeat biopsy. The diagnosis of ASAP is trending towards a lower incidence in recent studies ranging from 0.7-23.4% (mean=5%, median=4.4%).[12] In this study, there were 2 cases of ASAP (Table 1), but none of them turned up for a repeat biopsy.

Eosinophilic crystalloids are dense eosinophilic structures that assume various shapes such as rhomboid or needle seen in the lumen of glands, which are commonly seen in cancer, but also in benign lesions.[13] In our study, there was only 1 case of cancer, which showed eosinophilic crystalloids (3.3% among the malignant cases, Table 3), but none of the other malignant or benign cases showed such structures.

In this study, although there is no support of molecular study, 1 case of high-grade prostate cancer with high Gleason score (5+4=9) showed features of Intraductal Carcinoma of the Prostate (IDC-P) (Table 3). The concept of IDC-P is emerging and is characterised by non-confluent yet crowded proliferation of large cribriform glands lined by pleomorphic malignant cells with or without necrosis and with partial or complete basal cell lining. In the low-grade spectrum, IDC-P is morphologically similar to cribriform HGPIN, but molecular study demonstrates TMPRSS2-ERG gene fusion in 75% of IDC-P cases supporting that the two lesions are distinct entities.

In this study, glomerulation was assigned a Gleason grade 4. There were 4 cases, which showed features of glomerulation (Table 3) and all were found associated with intermediate to high Gleason score. A recent study by Lotan TL et al[14] have suggested to assign it a Gleason grade 4 because the adjacent carcinoma frequently demonstrates grade 4 cribriform glands. Our findings of glomerulation associating with a high Gleason grade was similar to other studies.

Corpora amylacea are round, concentrically laminated structures within the lumen of prostate glands. Christian JD et al[15] have found it to be associated more with benign lesions and concluded that they are rarely seen in prostate cancers and that their presence usually mitigates against a cancer diagnosis. In our study, we found 1 (3.3%) case out of 30 prostate cancers (Table 3) and 12 (75%) cases out of 16 benign cases to be associated with corpora amylacea.

In this study, there were 10 cases with cribriform pattern, among 30 malignant cases, of which 9 (90%) cases and 1 (3.3%) case showed cribriform grade 4 and grade 3 patterns respectively (Table 3). Cribriform grade 3 glands are smooth well circumscribed and are of the same size as the benign glands, whereas cribriform grade 4 glands are larger with irregular outlines, however, when associated with necrosis, they are assigned grade 5. Amin MB et al[16] have highlighted that a vast majority of cribriform pattern in needle biopsies are cribriform grade 4 (95%), which is similar to our study.

Prostatic adenocarcinoma with ductal differentiation or ductal adenocarcinoma, previously known as endometrial or endometrioid carcinoma is seen as pure ductal carcinoma or mixed ductal and acinar morphology and has incidence of 1.3% and 5% respectively in needle biopsies. Pure ductal carcinomas are more aggressive, usually present at a more advanced stage and are now regarded as Gleason grade 4 or 5 when associated with necrosis. Unlike the pure form, mixed form or carcinoma with ductal differentiation has a prognosis comparable to usual acinar carcinoma. In our study, there was 1 (3.3%) case of carcinoma having ductal differentiation (Table 3) with Gleason score 4+4=8 and is concordant with other studies.[17,18]

In this study, out of 30 malignancies, there were 2 (6.7%) prostatic carcinomas, which showed features of cystic atrophy (Table 3), it was noted in benign lesions also. Out of 16 benign cases, 5 (31.25%) patients showed features of cystic atrophy. Prostate carcinomas with cystic atrophic were found in 24% cases in a study of 385 patients with prostatic carcinoma[19] and 70% of men in their 2nd and 3rd decades have features of atrophy.[20] The possible reason for this discordance maybe a difference in the sample sizes.

Stromal nodule of myogenous type was found in 1 (6.25%) case among the 16 benign lesions. This finding is consistent with other studies. Bierhoff E et al[21] have studied 475 cases of benign prostatic hyperplasias and found 4 types of stromal nodules namely, immature mesenchyme, fibroblastic, fibromuscular and myogenous. The percentages of each type in their study were 8.8%, 65.2%, 21.6 and 4.4%, respectively.

The significance of prostatitis as a causative factor for BPH was mentioned in different literatures and attempts were made to classify chronic prostatitis. In this study, 2 cases of BPH showed features of chronic prostatitis where the amount of inflammatory cells was mild having a multifocal periacinar distribution. Blumenfeld W et al[22] stated that adult prostate have patchy mild acute and chronic inflammation. When the inflammation is severe, extensive and clinically apparent, the term prostatitis is warranted, a majority of which caused by bacterial infection. Further, it is appropriate to classify prostatitis into acute and chronic prostatitis. Kramer G and Marberger M[23] have mentioned inflammation as one of the factors in the pathogenesis of benign prostatic hyperplasia where increased expression of IL-6, IL-8 and IL-17 stimulate fibromuscular growth through autocrine or paracrine effect or through expression of COX-2. Nickel JC et al[24] have made a proposal on histologic classification of prostatitis according to location, extension and grade.

Out of 16 benign cases, there was 1 (6.25%) case of granulomatous prostatitis (Table 1) with serum tPSA value of 21.3 ng/mL. The incidence of granulomatous prostatitis in this study was similar with that of Epstein JI and Hutchins GM[25] where they found it to constitute 1.2% of all prostatectomy specimens.

Adenocarcinoma associated with an elevated serum tPSA is more likely to have higher Gleason score, larger tumour volume and more advanced pathologic stage. Blackwell KL et al[26] found significant positive correlation between serum tPSA and Gleason score. In this study also, there was a good correlation between serum tPSA and Gleason grade (r_s=0.908), which was found to be statistically significant (p=0.000) (Figure 2).

In this study, it was found that there is an increasing trend of tPSA values from benign to premalignant and malignant cases. Statistical analysis using one-way ANOVA test showed this to have a good correlation (r_s = 0.908) with a high degree of significance (p=0.000) (Table 2). Similar studies by Lakhey M et al[27] and Blackwell KL[26] showed correlation between tPSA with benign and malignant cases, but not with premalignant cases. The possible reason for non-concordance with their study maybe due to a lesser number of premalignant cases (4 cases) in this study.

Tomioka S et al[28] did a concordance study of Gleason grade in needle biopsies and matched prostatectomy specimens, which included 223 cases and exact correlation of Gleason grade was found in 37%. They also found under-grading (40%) and over-grading (33%) of Gleason scoring on needle biopsies. In our study, 7 cases of prostate cancer on biopsy would correlate well with corresponding prostatectomy specimens and it was found that the percentage of exact correlation and under-grading of Gleason grade were 85.48% and 14.28%, respectively. There were no cases of over-grading of Gleason grade. The possible reason for the discrepancy between their study and this study maybe due to difference in the sample sizes.

CONCLUSION

Prostate cancer is one of leading cause of cancer morbidity and mortality among the elderly males. The advancement of newer technologies like MRI and use of serum tPSA as a screening tool have made it possible to identify the disease at an earlier stage and has also resulted in an increased detection rate. Although, more number of cases are detected at earlier stage, yet there is no marker to predict the disease course and at times this leads to unnecessary overtreatment. Image-guided prostate biopsy is a daycare procedure and has a good compliance in most cases.

In the present study, maximum number of cases were that of malignancies. Among the malignant cases, well-differentiated or low-grade ones constituted the maximum number. When comparing the grading system of biopsies with that of the corresponding prostatectomy specimens, all except one were matched. Although, benign cases constituted a minority in this study, PIN, stromal nodule and granulomatous lesion were important pathological findings.

While literatures have claimed that MRI can distinguish benign from malignant lesions of prostate accurately, the age old 'histopathology', still remains the gold standard. As far as the procurement of representative material is concerned, the role of image-guided biopsy has added advantages, namely relatively safe and inexpensive being an OPD procedure with less complications having better patient tolerance and without having a need for general anaesthesia.

REFERENCES

[1] Magi-Galluzzi C, Zhou M, Epstein JI. Non-neoplastic diseases of the prostate. In: Zhou M, Magi-Galuzzi C, Goldblum JR, eds. Genitourinary pathology. China: Churchill Livingstone 2007:1-4.
[2] Shah RB, Zhou M. Prostate biopsy interpretation: an illustrated guide. Berlin: Springer 2012.
[3] Bostwick DG, Qian J, Hossain D. Non-neoplastic diseases of the prostate. In: Bostwick DG, Cheng L, eds. Urologic surgical pathology. 2nd edn. New York: Elsevier 2008:384-386.
[4] Population Based Cancer Registry, Manipur State. Regional Institute of Medical Sciences, Imphal. Individual registry write-up: 2006-2008. http://www.canceratlasindia.org/
[5] Scher HI. Benign and malignant diseases of the prostate. In: Longo DL, Fauci AS, Kasper DL, et al, eds. Harrison's principles of internal medicine. 18th edn. New York: Mc Graw-Hill 2012:796-797.
[6] Catalona WJ, Richie JP, Ahmann FR, et al. Comparison of digital rectal examination and serum prostate specific antigen in the early detection of prostate cancer: results of a multicenter clinical trial of 6,630 men. J Urol 1994;151(5):1283-1290.
[7] Thorson P, Vollmer RT, Arcangeli C, et al. Minimal carcinoma in prostate needle biopsy specimens: diagnostic features and radical prostatectomy follow-up. Mod Pathol 1998;11(6):543-551.
[8] Weight CJ, Ciezki JP, Reddy CA, et al. Perineural invasion on prostate needle biopsy does not predict biochemical failure following brachytherapy for prostate cancer. Int J Radiat Oncol Biol Phys 2006;65(2):347-350.
[9] Pacelli A, Lopez-Beltran A, Egan AJ, et al. Prostatic adenocarcinoma with glomeruloid features. Hum Pathol 1998;29(5):543-546.
[10] Epstein JI, Herawi M. Prostate needle biopsies containing prostate intraepithelial neoplasia or atypical foci suspicious for carcinoma: implications for patient care. J Urol 2006;175(3 Pt 1):820-834.
[11] Leftkowitz GK, Taneja SS, Brown J, et al. Followup interval prostate biopsy 3 years after diagnosis of high grade prostate intraepithelial neoplasia is associated with high likelihood of prostate cancer, independent of change in prostate specific antigen levels. J Urol 2002;168(4 Pt 1):1415-1418.

[12] Iczkowski KA, MacLennan GT, Bostwick DG. Atypical small acinar proliferation suspicious for malignancy in prostate needle biopsies: clinical significance in 33 cases. Am J Surg Pathol 1997;21(12):1489-1495.
[13] Henneberry JM, Kahane H, Humphrey PA, et al. The significance of intraluminal crystalloids in benign prostatic glands on needle biopsy. Am J Surg Pathol 1997;21(6):725-728.
[14] Lotan TL, Epstein JI. Gleason grading of prostatic adenocarcinoma with glomeruloid features on needle biopsy. Hum Pathol 2009;40(4):471-477.
[15] Christian JD, Lamm TC, Morrow JF, et al. Corpora amylacea in adenocarcinoma of the prostate: incidence and histology within needle core biopsies. Mod Pathol 2005;18(1):36-39.
[16] Amin MB, Schultz DS, Zarbo RJ. Analysis of cribriform morphology in prostatic neoplasia using antibody to high-molecular-weight cytokeratins. Arch Pathol Lab Med 1994;118(3):260-264.
[17] Bostwick DG, Kindrachuk RW, Rouse RV. Prostatic adenocarcinoma with endometrioid features. Clinical, pathologic, and ultrastructural findings. Am J Surg Pathol 1985;9(8):595-609.
[18] Epstein JI, Woodruff JM. Adenocarcinoma of the prostate with endometrioid features. A light microscopic and immunohistochemical study of ten cases. Cancer 1986;57(1):111-119.
[19] Egan AJ, Lopez-Beltran A, Bostwick DG. Prostate adenocarcinoma with atrophic features: malignancy mimicking a benign process. Am J Surg Pathol 1997;21(8):931-935.
[20] De Marzo AM, Platz EA, Epstein JI, et al. A working group classification of focal prostate atrophy lesions. Am J Surg Pathol 2006;30(10):1281-1291.
[21] Bierhoff E, Vogel J, Benz M, et al. Stromal nodules in benign prostatic hyperplasia. Eur Urol 1996;29(3):345-354.
[22] Blumenfeld W, Tucci S, Narayan P. Incidental lymphocytic prostatitis. Selective involvement with non-malignant glands. Am J Surg Pathol 1992;16(10):975-981.
[23] Kramer G, Marberger M. Could inflammation be a key component in the progression of benign prostatic hyperplasia? Curr Opin Urol 2006;16(1):25-29.
[24] Nickel JC, True LD, Krieger JN, et al. Consensus development of a histopathological classification system for chronic prostatic inflammation. BJU Intl 2001;87(9):797-805.
[25] Epstein JI, Hutchins GM. Granulomatous prostatitis: distinction among allergic, nonspecific, and post-transurethral resection lesions. Hum Pathol 1984;15(9):818-825.
[26] Blackwell KL, Bostwick DG, Myers RP, et al. Combining prostate specific antigen with cancer and gland volume to predict more reliably pathological stage: the influence of prostate specific antigen cancer density. J Urol 1994;151(6):1565-1570.
[27] Lakhey M, Ghimire R, Shrestha R, et al. Correlation of serum free prostate-specific antigen level with histological findings in patients with prostatic disease. Kathmandu Univ Med J 2010;8(30):158-163.
[28] Tomioka S, Nakatsu H, Suzuki N, et al. Comparison of Gleason grade and score between preoperative biopsy and prostatectomy specimens in prostate cancer. Int J Urol 2006;13(5):555-559.