Study of Various Histopathological Patterns in Turp Specimens and Incidental Detection of Carcinoma Prostate

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ABSTRACT

Background (Aims and Objective): *Study of various histopathological patterns in TURP specimens diagnosed as Benign Prostatic Hyperplasia, identifying type and grade of inflammation, incidental detection of carcinoma prostate and application of modified Gleason system.*

Materials and Methods: *From January 2014 to August 2015 a total of 50 TURP specimens were evaluated. The tissue blocks and H&E stained slides of the tissues were retrieved and slides reviewed. Various patterns of proliferation, types and grade of inflammation were studied and classified using standard methods. Incidentally identified carcinoma prostate were classified using WHO Classification and graded using modified Gleason system.*

Results: *48(96%) were BPH with co-existing chronic prostatitis 12(24%) granulomatous prostatitis 1(2%) and acute prostatitis 2(8%). Papillary hyperplasia was predominant finding 17(34%). Less frequent finding was basal cell hyperplasia, 6(12%) atypical adenomatous hyperplasia 4(8%) and cribriform hyperplasia 1 (2%). Proliferative inflammatory atrophy constituted 3 cases(6%).Scattered necrotic glands were present in 20(40%) cases, periglandular lymphoid aggregation was a frequent finding in these necrotic glands. we reported two cases of adenocarcinoma prostate with modified Gleason score of one (5+4=9) and another score of (5+3=8).*

Conclusion: *With increase in the incidence and mortality rates from prostate cancer, every effort should be made to improve diagnosis. It is necessary to review periodically all TURP in order to identify premalignant lesions, proliferative activity, and grade of inflammation. Efforts should be made to apply modified Gleason system to improve management facility. We also conclude that proliferative activity and invasiveness increases from benign to the malignant end in the spectrum of prostatic lesion.*

Keywords: *Benign Prostatic Hyperplasia, Prostate Carcinoma, Aah, Pia, Chronic Prostatitis.*

INTRODUCTION

Prostate is fibromusculoglandular organ encircling the neck of the urinary bladder. So, enlargement or growth of prostate due to nodular hyperplasia or prostatic intraepithelial neoplasia or adenocarcinoma may give rise to bladder outlet obstruction[1]

Benign prostatic hyperplasia is an extremely common condition in men over the age of 50 years and shows remarkable racial and geographical variations in incidence and mortality[2].Within the last two decades, there has been a sudden increase of interest in diseases of prostate largely due to the perceived high incidence of prostate cancer in different geographical and ethnic groups globally[3].Of the diseases which affects the prostate the most frequently encountered in clinical practice are Benign prostatic hyperplasia, prostatic cancer and prostatitis[4].Recently premalignant lesions have become defined, largely as result of advances in technology. Therefore in the light of growing knowledge of prostatic lesions, it is necessary to periodically review known benign lesions in order to reassess any relationship or impact they may have on malignant or premalignant prostatic disease[5].Benign Prostatic Hyperplasia (BPH) is a histological diagnosis associated with unregulated proliferation of connective tissue, smooth muscle and glandular epithelium with in the prostatic transition zone.[6]

Non-specific granulomatous prostatitis is noticed occasionally in prostate specimen. It was first described by Tanner and Mc Donald in 1943, who reported an incidence of 3.3% of granulomatous prostatitis in inflammatory lesions. Harsh Mohan et al studied 20 cases of granulomatous prostatitis, of which two were the cases of tuberculous prostatitis[7].Proliferative changes of epithelium are linked to carcinogenesis in almost all epithelial malignancies. Proliferative regenerative change, referred to in the prostate as proliferative inflammatory atrophy(PIA), has been postulated as a

Access this article online	
Quick Response Code:	Website: www.innovativepublication.com
	DOI: 10.5958/2394-6792.2015.00032.0

premalignant lesion. The hypothesis is that cellular injury and regeneration characteristic of PIA is induced by inflammation and release of reactive oxygen species(oxidative stress) resulting from insult owing to chemicals (e.g., dietary carcinogens), or bacteria. The regenerating cells are at increased risk of mutation which, in turn, predisposes them to cancerous initiation, promotion, and progression.[8] Atypical adenomatous hyperplasia(AAH) is a localized proliferation of small glands with in the prostate that may be mistaken for carcinoma. Features that could not reliably separate AAH from carcinoma include lesion shape, circumscription, multifocality, average gland size, variation in gland size and shape, chromatin pattern and amount and tinctorial quality of cytoplasm. Although the biologic significance of AAH is uncertain, its light microscopic features allow it to be distinguished from carcinoma in most cases.[9]

Prostatic carcinoma is globally the second most frequently diagnosed cancer and the sixth leading cause of cancer death in males**.** In India, it constitutes about 5% of all male cancers.[10]The modified Gleason system appears to better predict progression –free survival after radical prostatectomy than the original Gleason system did. Prior to the PSA era, up to 27% of prostate cancers were detected incidentally at the time of TURP[11]. The histochemistry for the mucins of the prostate has proved to be immensely helpful, especially in demonstration of somewhat cancer specific acid mucin.[12]Limitation of study: we were not able to perform immunohistochemistry, tumor markers as the group belongs to below poverty line.

MATERIAL AND METHODS

From January 2014 to August 2015 a total of 50 patients who underwent TURP were evaluated, the tissue blocks and H&E stained slides of the tissues were retrieved and slides reviewed. Various histopathological patterns were studied in all cases and were classified with reference to age. Following histologic assessment, the tumors were classified according to WHO recommendation, and histologic grading was done using modified Gleason system.

Pathologic review

Following parameters were specifically examined.

1) **Histological patterns:** Patterns were categorized as "glandostromal" where there was excess glandular proliferation over stromal, or where proliferating glands and fibromuscular stroma were assessed to be roughly in equal proportion. Where the sections showed more stromal elements than glands or were made up almost entirely or entirely of stromal elements were designated as "stromal"
2) **Prostatitis:** Inflammatory change with in prostate glands were separated into acute and chronic

Acute: Neutophils with in glands

Chronic:

A. Non specific; mononuclear infiltrate.

B. Granulomatous.

3) **Necrotic glands:** The presence or absence of individually necrotic glands was noticed. These glands were almost invariably surrounded or replaced by a localized inflammatory infiltrate.
4) **Types of epithelial hyperplasia:** Various hyperplastic lesions were examined which were seen predominantly in glandular pattern followed by glandulostromal pattern, and classified them into Papillary, Basal, Cribriform.
5) **Atypical adenomatous hyperplasia (AAH).** The presence of atypical hyperplasia was defined using the criteria of Epstein [13]. Briefly, it is nodular focus of proliferating, newly formed acini or alveoli about a duct branch. It consists of proliferation of small acini with in a duct-acinar unit. The cells are cuboidal to columnar secretory epithelial cells, often with clear cytoplasm and little or no nuclear pleomorphism.
6) **Proliferative inflammatory Atrophy:** Atrophy was categorized following the system developed by De Marzoet al[14](simple atrophy; post-atrophic hyperplasia; simple atrophy-cyst formation; partial atrophy). The extent of inflammation (focal, multifocal, diffuse) grade (mild, moderate, and sever) of inflammation was assessed according to the criteria proposed by Nickle et al [15]**.**
7) **Carcinoma Prostate:** Carcinoma prostate was identified incidentally in two TURP samples and were classified depending on morphology and modified Gleason Grading done according to the 2005 International Society of Urological Pathology modified Gleason system[16]
8) **Application of Alcian blue stain in BPH and Carcinoma prostate:** 50 blocks which were retrieved were then cut into sections of 5 micron thickness, and were subjected to Alcian blue stain at PH 2.5 and bluish black nuclei along with the blue colored acid mucin were observed.

RESULTS

The present study constituted a total of 50 cases. All prostatic specimens were broadly classified into non neoplastic 48(96%) and neoplastic 2(4%). Each category was then subclassified into specific types according to standard classification systems. The age distribution of neoplastic and non neoplastic lesion is depicted in **table 1**.

BPH was the most frequent finding and was observed in 48(96%). Maximum number of lesions were seen in the age group of 61 to 70 (correlated

well with the study by Garg M et al). With an average age at presentation of 65 years. A glandulostromal pattern of hyperplasia**(FIG.1)** was the most frequent histological pattern which occurred. Stromal pattern of hyperplasia was less common. BPH was associated with acute prostatitis in 2(4%)**(FIG.4)** chronic prostatitis**(FIG.3)** in 12(24%), Granulomatous prostatitis is noticed occasionally in prostate specimens. In this study we report one (2%) case of granulomatous prostatitis which showed granulomas with Langhan's giant cells and foci of necrosis; however, Ziehl Nelsen staining was negative for AFB, and is labeled as non specific. Basal cell hyperplasia in 6(12%) papillaryhyperplasia in 17(34%), atypical adenomatous hyperplasia **(FIG.2)** in 4(8%), **(TABLE-3)**. Proliferative inflammatory atrophy (PIA) **(FIG.6)** in 3(6%). Scattered necrotic glands**(FIG.5)** were present in 20(40%) cases, periglandular lymphoid aggregation was a frequent finding in these necrotic glands, ranging in intensity from scattered lymphocytes to well- formed lymphoid follicles. In few cases necrotic glands were confluent.**(TABLE-2)** We reported two cases of Prostatic adenocarcinoma accounting for 2 neoplastic lesions (100%) Case no one with age of 53 presented with urinary tract obstruction. Histopathology of TURP received showed loss of glandular differentiation composed of solid sheets, cords and single cells, with features such as nuclear enlargement and hyperchromasia. (modified Gleason grade 5) **(FIG. 8)**. Second most predominating pattern is large clear cells growing in a diffuse pattern with occasional gland formation. (modified Gleason grade 5+4=9).

In second case the age of 70 presented with same clinical presentation, histopathology of TURP showed more predominant pattern of various sizes of glands which infiltrate into surrounding stroma. Majority of glands were small in size. (modified Gleason grade 3) second most predominant pattern is sheets of neoplastic cells pleomorphic, having hyperchromatic mucleus.**(FIG.11)**(modified Gleason grade 5+3=8).

None of BPH cases positive for Alcian blue staining (fig-9) meanwhile, Alcian blue positive for acidic mucin was observed in both adenocarcinoma prostate.**(FIG.7&10)**.

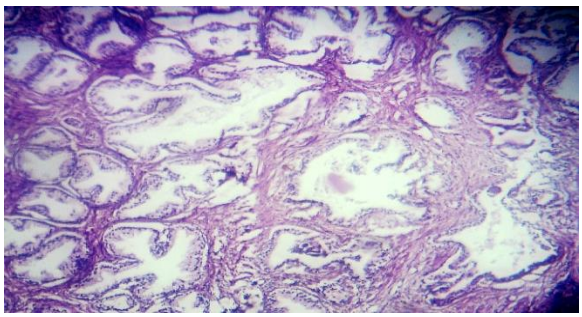

Fig. 1: BPH. BPH(H&E stain) (10X Magnification)

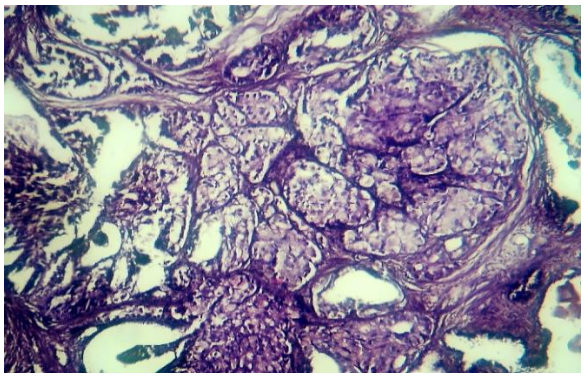

Fig. 2: AAH. AAH(H&E stain) (40X Magnification)

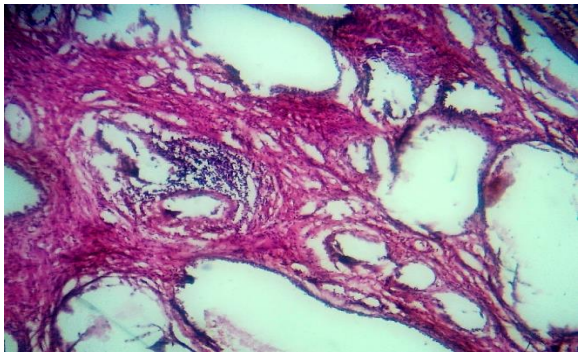

Fig. 3: LYM. Lymphoid aggregate(H&E stain) (10X Magnification).

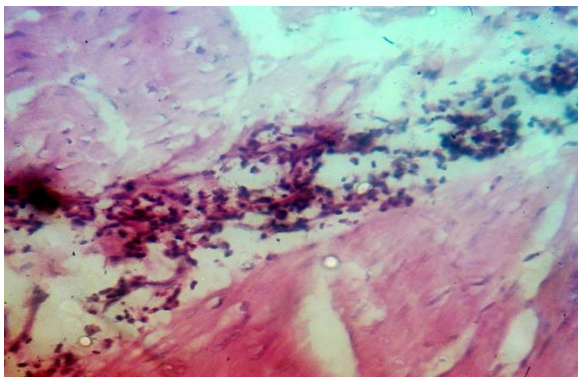

Fig. 4: Neuet. Neutrophilic Infiltrate(H&E stain) (40X Magnification).

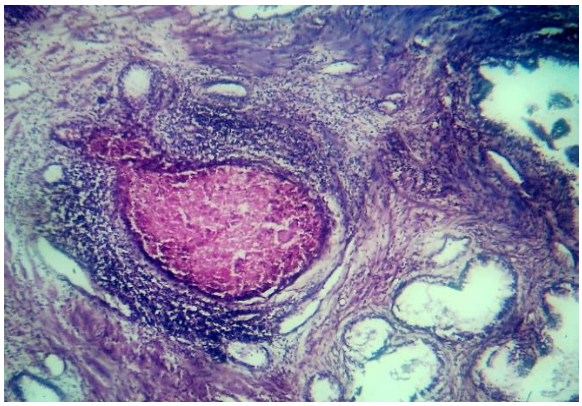

Fig. 5: NECC. Lymphoid aggregate around necrotic foci (H&E stain) (10X Magnification).

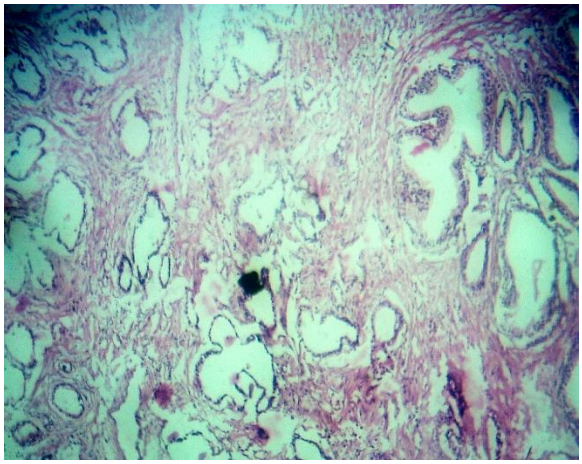

Fig. 6: PIA. Proliferative Inflammatory Atrophy(H&E stain) (10X Magnification).

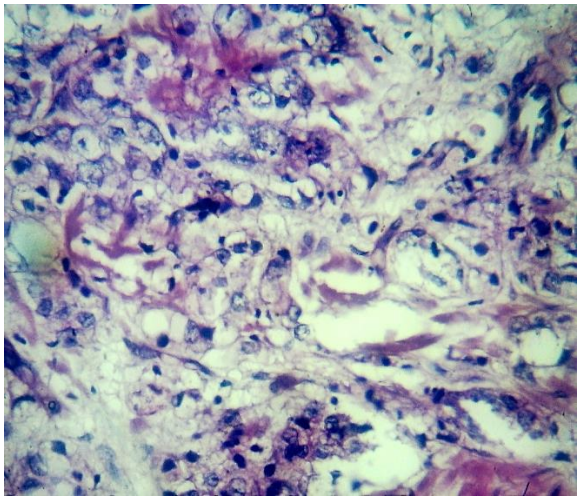

Fig. 7: alcianbl +. Positive Alcian Blue in carcinoma Prostate(H&E stain) (10X Magnification).

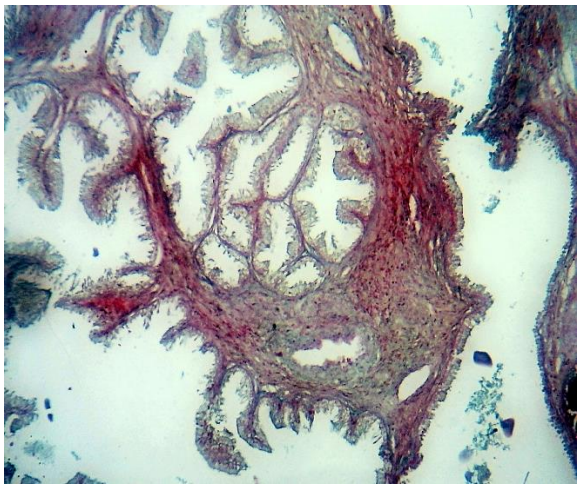

Fig. 8: 15192 H&E. Carcinoma Prostate (H&E stain) (40X Magnification).

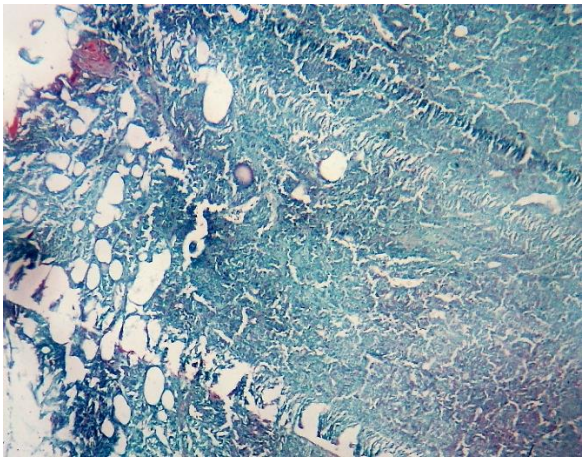

Fig. 9: NEG AL BPH. Negative Alcian Blue in BPH(H&E stain) (40X Magnification).

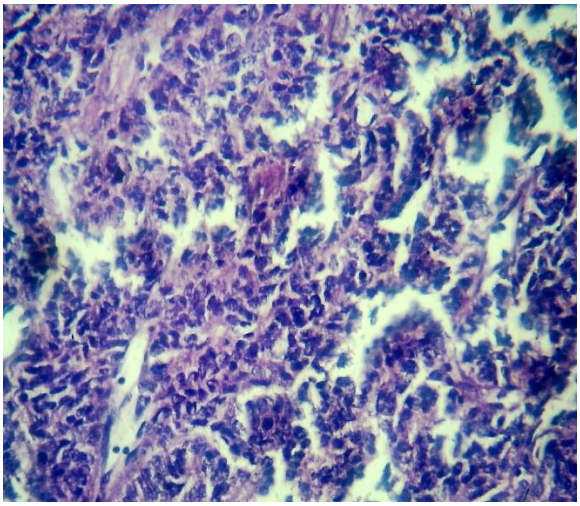

Fig. 10: AL +2ND. Positive Alcian Blue in carcinoma Prostate (H&E stain) (10X Magnification.).

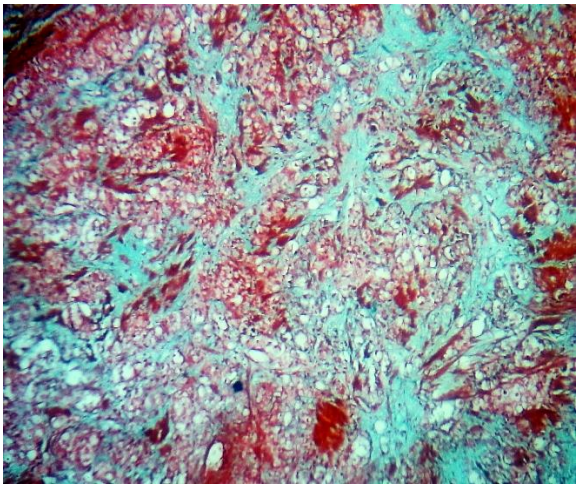

Fig. 11: 15204 H&E. Carcinoma Prostate (H&E stain) (40X Magnification).

Table: 1

Age (yr)	Non Neoplastic, n(%)	Neoplastic n(%)
40-50	3(6%)	
50-60	15(30%)	01(2%)
61-70	21(42%)	01(2%)
71-80	8(16%)	
81-90	1(2%)	
Total	48	02(4%)

Table 2

VARIABLE (inflammation)	No of Cases	Necrosis (No of cases)
A.Type of Inflammation present		
1) Acute	2	3(6%)
2) Chronic	12	
B.Grade of inflammation		
1) none	4	
2) mild	31	1(2%)
3) moderate	11	9(18%)
4) sever	4	10(20%)
C. Extent of inflammation		
1) none	4	
2) focal	31	
3) multifocal	11	
4) diffuse	4	
D. Granulomatous inflammation	1	
E. Proliferative inflammatory Atrophy	3	

Table 3

Type of hyperplasia					
Glandular				Glandulo stromal	stromal
Papillary	Basal	cribriform	AAH		
17(34%)	6 (12%)	1(2%)	4 (8%)	20(40%)	4 (8%)

DISCUSSION

This study shows interesting associations and relationships among various observed parameters in BPH that bears reiteration. We observed that 96% of total (50 cases) were benign and 4% malignant lesion occurring on a ratio of 24:1 exactly in the middle compare to study in Nigeria[17]where the ratio is 3:1 and compared to reports from Sudan where the ratio is 49:1[18].

This study confirms earlier reports from regions of Nigeria and other African countries where the BPH incidence was found to reach its peak in the 7th decade. The histologic subtypes of BPH encountered agree with a similar study on benign disorders of the prostate in Kuwait[5] and histopathological pattern of prostatic diseases in Nigeria[17] where the majority of cases had a glandulostromal pattern. Similarly, chronic prostatitis was found to co-exist with BPH in about one quarter of the cases reviewed, which is not too different from other similar study. However the proportion of cases with acute prostatitis (4%) almost similar with study in Nigeria where (2.1%) of cases had acute prostatitis and differed remarkably from findings in Kuwait where 49.1% had acute prostatitis. The variation is likely due to various criteria used in assessing prostatitis. In general, prostatitis is detected in 11-98% of prostatic specimens depending on the diagnostic criteria used.[19].

Papillary hyperplasia was the most common observed epithelial hyperplasia. The epithelial changes found in BPH have been described by several workers.[5]The prevalence of AAH in TURP specimens without cancer ranges from 1.6% to 7.3%. AAH is most often located in transition zone of the prostate in intimate association with benign nodular hyperplasia.[20]

The exact etiology of Granulomatous prostatitis remains unclear and may in many cases be idiopathic. The prevalence of prostatic carcinoma in present study was (4%) i.e., 2 of 50 cases. Close to previous study by Otto B et al[21]where only 1.4% patients were found to have prostate cancer on pathology.

Adenocarcinoma was the only histological type of cancer found in this study just like other parts

of world where Adenocarcinoma was the most common type.[17] With respect to Alcian blue staining in prostate cancer samples, the findings from this study are in line with previous reports, which demonstrate the presence of acid mucin secretions to be more frequent in malignant versus benign prostate lesion. However in contrast to previous reports acid mucin is demonstrated in malignant cells with higher grades.[12]

CONCLUSION

With increase in the incidence and mortality rates from prostate cancer, every effort should be made to improve diagnosis. It is necessary to review periodically all TURP in order to identify premalignant lesions, proliferative activity, grade of inflammation. Efforts should be made to apply modified Gleason system so as to improve management facility. We also conclude that proliferative activity and invasiveness increases from benign to the malignant end in the spectrum of prostatic lesion. Application of histochemistry was an added advantage to differentiate benign from malignant disorders especially in low socioeconomic areas.

Conflict of interest: NONE

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