IJPRP

Indian Journal of Pathology: Research and Practice 8(5) September - October 2019
DOI: http://dx.doi.org/10.21088/ijprp.2278.148X.8519.22

Original Research Article

Histomorphological Study of Premalignant Lesions of Prostate in TURP Samples

Swati Sahay[1], Aditya Vikram Singh[2], Sateesh Jighjini[3]

[1,2]Post graduate student [3]Professor, Dept. of Pathology, S Nijalingappa Medical College, HSK (Hanagal Shree Kumareshwar) Hospital and Research Centre, Bagalkot, Karnataka 587102, India.

Corresponding Author:

Aditya Vikram Singh, Post graduate student, Dept. of Pathology, S Nijalingappa Medical College, HSK (Hanagal Shree Kumareshwar) Hospital and Research Centre, Bagalkot, Karnataka 587102, India.

E-mail: swatisahay16@gmail.com
adi.Knight@gmail.com

Received on 05.07.2019,

Accepted on 16.08.2019

Abstract

Carcinoma prostate falls next to carcinoma lung in incidence and mortality rate. With increasing age of men incidence of prostatic carcinoma is seen to be increasing. In recent years significant achievement is made in early diagnosis and the detection of carcinoma prostate. Technologies such as immunohistochemistry, flow cytometry, fluorescent in situ hybridization (FISH) have helped in the study of premalignant and malignant lesions of prostate. Concept of Intra epithelial development of carcinoma progressing to invasive is a well-recognised phenomenon with cervical cancer, oral cancer and so also the carcinoma Prostate. Orteil in 1926 gave the first description of premalignant changes in the prostate. The premalignant lesions of prostate include prostatic intraepithelial neoplasia (PIN) and atypical adenomatous hyperplasia (AAH) and recently, the new lesion added to the list of premalignant lesion is proliferative inflammatory atrophy (PIA). Screening for prostate cancer is controversial. Although the past several decades have seen declines in overall prostate cancer mortality, some evidence exists that this is a function of improved survival for men with advanced prostate cancer rather than men with early-stage disease who presumably would benefit from screening. It is recommended by-American Urological Association that in general, men 50 years and older with a reasonable certainty of a 10-year life expectancy should be screened annually or biennially. Patients with an elevated risk of disease (e.g., African Americans and those with a family history) should be screened beginning at an earlier age (45 years). In this part of our country the socio-economic conditions and the facilities pose limitations for people screening to be undertaken. In clinical practice, AAH, HGPIN and PIA remains undetected as most of these lesions does not reveal any abnormality on clinical (digital rectal examination), biochemical (PSA level analysis and radiological (trans rectal ultrasound) evaluation. Hence, histopathology remains the gold standard for diagnosis of these putative precursor lesions of prostatic carcinoma. Identification of these lesions of prostate will help in early detection of carcinoma and guide the urologist for appropriate management of the patient.

Keywords: BPH; PIN; CARCINOMA; P63; AMACR.

How to cite this article:

Swati Sahay, Aditya Vikram Singh, Sateesh Jighjini. Histomorphological Study of Premalignant Lesions of Prostate in TURP Samples. Indian J Pathol Res Pract. 2019;8(5):661–65.

Introduction

Transurethral resection of prostate and prostatic biopsies are very common specimens in surgical pathology. Prostatic biopsies are done in cases where there is clinical suspicion of malignancy. These specimens have to be thoroughly examined to avoid false negative diagnosis of adenocarcinoma prostate. Non-neoplastic lesions which are to be distinguished from adenocarcinoma prostate are atrophy including partial atrophy, atypical adenomatous hyperplasia (adenosis), crowded benign glands, sclerosingadenosis, radiation atypia in benign glands, basal cell hyperplasia, clear cell cribriform hyperplasia, non-specific granulomatous prostatitis, dense inflammation and malakoplakia, In recent years significant achievement is made in early diagnosis and the detection of carcinoma prostate.[5]

Concept of Intra epithelial development of carcinoma progressing to invasive is a well-recognised phenomenon with cervical cancer, oral cancer and so also the carcinoma Prostate.[1]

Orteil in 1926 gave the first description of premalignant changes in the prostate. The premalignant lesions of prostate include prostatic intraepithelial neoplasia (PIN) and atypical adenomatous hyperplasia (AAH) and recently, the new lesion added to the list of premalignant lesion is proliferative inflammatory atrophy (PIA).[6]

Objectives of The Study:

1. To study morphological features of Premalignant lesions. of prostate
2. To apply Gleason's criteria and group premalignant lesions.

Scope of Objectives

1. Studying morphological features of PIN by H&E stains and by immunohistochemistry using P63 and AMACR and classifying the lesions as LGPIN and HGPIN.
2. Studying PIN associated with Incidental carcinoma and grouping the lesions based on Gleason's score applied to carcinoma component.

Materials and Methods

Total 100 samples of TURP were studied at the Department of Pathology. S. Nijalingappa Medical College HSK Hospital for a period of 18 months from December 2016 to May 2018. Calculated sample size of 70 was increased to 100 because of availability of samples over the period of 18 months.

The sample size was calculated by statics was minimum 70 which was calculated by the formulae using Open version 2.3.1. it was extended further to 100 because of availability

According to study conducted by Rekhi. *et al*[6]. The proportion of neoplastic lesion in prostate is found to be 86.9%= *p* at 95% confidence limit with a relative precision of 8%.

Type of study: Case series study

Inclusion Criteria

- All TURP specimens
- All TURP specimens diagnosed as Prostate Intraepithelial Neoplasia, (PIN) atypical adenomatous hyperplasia, and Proliferative inflammatory atrophy.

Exclusion Criteria:

- Un preserved Samples
- Benign mimics of malignancy where there is breech in basement membrane.
- Invasive Carcinomas not associated with PIN

A total of 100 cases were studied. Specimens included were TURP samples Written consent from all the patients posted for operation was obtained. The clinical history and other findings were recorded.

All TURP samples collected were fixed in 10% buffered formalin and then processed routinely.

Sections were stained with Haematoxylin and Eosin.

Results

The study was conducted on samples of TURP obtained 100 patients clinical data obtained and Histopathological examination was done.

Amongst the total of 100 cases, 86 cases (86%) were benign, 14 cases (14%) were premalignant. 04 cases amounting to 4% were found to show PIN associated with incidental carcinoma. All these were showing High Grade PIN.

Age wise distribution of cases is shown in the Table 1. Youngest patient was 39 Years old and the eldest was aged 90 Yrs. The maximum number of patients were in the age range of 61 to 70 years

Table 1: Age wise distribution of cases

Age (years)	Number of cases Total: 100	Percentage
<40 years	06	06%
41–50	17	17%
51–60	33	33%
61–70	37	37%
71–80	05	05%
81–90	02	02%

Table 2: Histopathological diagnosis observed in TURP

Diagnosis	Number of cases	% Value
BPH with prostatitis	44	44%
BPH without prostatitis	38	38%
LGPIN	10	10%
HGPIN	04	04%
Incidental carcinoma	04	04%

Table 3: Age wise distribution of Prostatic lesions.

Age	BPH With Prostatitis	BPH Without Prostatitis	Low Grade PIN	High GradePIN	Incidental Carcinoma	Total
<40	02	03	–	–	–	05
40–50	08	06	02	–	–	16
50–60	16	12	04	02	02	36
60–70	13	15	04	02	02	36
70–80	03	02	–	–	–	05
80–90	02	–	–	–	–	02
Total	**44**	**38**	**10**	**04**	**04**	**100**

Table 4: Clinical Presentation in Malignant and benign diseases

Clinical symptoms	Benign (86)	Pre+ Malignant (14)
Frequency of Inc micturition	86 (86%)	14 (14%)
Retention	23 (23%)	06 (6%)
Urgency	10 (10%)	02 (2%)
Feeling of residual urine	10 (10%)	02 (2%)
Painful initiation of micturition	10 (10%)	00

Table 5: Spectrum of lesions in TURP

Nodular hyperplasia		Low Grade PIN		High Grade PIN		Incidental carcinoma	
Cases	%	Cases	%	Cases	%	Cases	%
82	82%	10	10%	04	04%	04	4%

Table 6: Foci of Premalignant lesions in different categories

Category	Total no of cases	Number of positive cases	Premalignant condition %
1	10	10	10%
2	04	04	4%
3	–	–	–
Total	**14**	**14**	**14%**

(37%).

A total of 100 TURP samples were studied and categorised into three categories using the criteria described by Rekhi *et al* [4] (Tables 3-10).

Category 1- Nodular hyperplasia and associated premalignant condition.

Category 2- Adenocarcinoma and premalignant condition.

Category 3- Nodular hyperplasia with adenocarcinoma and premalignant condition together.

Table 7: Showing various architectural pattern in HGPIN

Pattern of HGPIN	No. of cases	% of cases
Cribriform	02	14.28%
Tufting	02	14.28%
Micropapillary	00	–
Flat	00	–

Table 8: Showing various Gleasons pattern in Incidental carcinoma

Gleaso pattern	Primary No. of cases	Secondary No. of cases	Tertiary No. of cases
1	00	00	00
2	00	00	00
3	02	02	00
4	02	00	00
5	00	02	00

Table 9: Showing Gleason's scoring in Incidental carcinoma with PIN

Gleason score	No. of cases	% of cases	Differentiation
6	00	00	–
7	02	14.28%	Moderately diff
8	02	14.28%	Poorly diff
9	00	00	–
10	00	00	–

Table 10: Showing% of cases showing P63 and AMACR positive in PIN and carcinoma

	LGPIN		HGPIN		Incidental Carcinoma	
IHC marker	No of cases-10	% case 10%	No. of cases-04	% case 4%	No of cases -04	% case 4%
P63	All positive		Focally disrupted		Absent	
AMACR	Negative		Weakly positive		Strongly positive	

Discussion

Literature review reveals that the term PIN was introduced in 1987 by Bostwick.[11] Initially It was described in three grades which later was merged in to two grades namely as Low grade PIN (LGPIN) and high grade PIN (HGPIN). Cellular features, their arrangements and the nuclear features formed basis for this grading. Various features described are cell crowding, stratification, nuclear enlargement, pleomorphism, chromatin pattern and nucleolar appearance. Reported prevalence of LGPIN varies considerably in different studies. It ranges from 3.7% to 12.3%.

In a study conducted by Rekhi *et al*.[4] they reported 29.9% of PIN in BPH in prostatetectomy specimens and expressed in their discussion that supportive evidence for PIN is much greater than AAH, with high-grade PIN being the most likely precursor, arising in the peripheral zone Our study the incidence of 14% of PIN which is significantly lower that the observation of Rekhi *et al*.[4] The TURP specimens usually represent central zone. and therefore the incidence of 14% of PIN may not match the observed finding of 29.9% PIN in their study. In our study we had 4 cases of coincident carcinoma amounting to (4%) as against the observation of Fredrik J. Skjørten *et al*.[24] which is of 58.27% The mean age reported by them and that of ours are similar. This may be because

of the larger number of samples collected and studied by double blind study. Their statistics show that out of 731 TURP specimens 426 showed PIN (58.27%) They reported PIN 1 in 8%, PIN 2 in 29%, and PIN 3 in 21%. Considering the reference of skjorten PIN 2 and PIN 3 to form HGPIN their statistics for LGPIN and HGPIN would be 8% and 50%.[30]

The study showed by Sharma *et al.*[28] showed 8 cases of incidental carcinoma whereas in our study we had observed 04 cases of incidental carcinoma. They noted 5.71% of PIN as against our record of 14%. which is slightly higher than our study. They concluded that BPH was most common and PIN is relatively uncommon to which our observation agree. All prostate carcinoma were In a study by Laxmibai *et al.*[15] LGPIN was seen in 12.3% and HGPIN 13.8% and in our study we observed 10% and 4% respectively in LGPIN and HGPIN. Our observations with respect to LGPIN are nearer to their observation while in case of HGPIN we differ. They concluded that HGPIN has high degree of association with carcinoma and Gleason's score of 8 to 10 is the most common score in their study and we recorded similar score amounting to 7 and 8. In our study we used p63 as a basal cell marker and AMACR for PIN lesions and adenocarcinoma prostate and revealed that p63 was focally disrupted in HGPIN and totally absent in adenocarcinoma prostate and AMACR was absent in benign hyperplasia of prostate, and positive in PIN lesions as well as in adenocarcinoma prostate.

The study conducted by Anand *et al.*[29] 40 suspicious cases were resolved by using two basal cell marker p63 and HMWCK and AMACR. Their study correlated with M.H Weistein *et al.* in which it is said that p63 is more superior to basal cell when compared to HMWCK. In our study we have also used both IHC marker to distinguish benign lesions from HGPIN and malignancy.

Conclusion

From the above study it is concluded that BPH remains the most common lesion in TURP and histopathology remains the gold standard for diagnosis of premalignant lesions.

HGPIN is the most common precursor lesion of carcinoma prostate hence the whole TURP samples should be submitted and biopsy is advised for better treatment outcome of the patient.

Hence, the focus of HGPIN, PIA and AAH should be highlighted by the pathologist and advised for close clinical follow-up with subsequent repeated re-biopsies which help in early detection and management of the patient.

Support: Nil

Conflicts of interest: Nil

Permissions: Nil

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