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Original Research Article

Premalignant Lesions and Incidental Carcinoma in Clinically Diagnosed Benign Prostatic Hyperplasia (BPH)

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Abstract

Background: Histological examination of the prostate must also include the description of some important aspects which are present associated with Benign Prostatic Hyperplasia(BPH) and which may condition the progression of the disease.

Aim: To find out incidence of Prostatic Intraepithelial Lesions (PIN) and incidental carcinoma in clinically diagnosed BPH, and to correlate histological findings with patients age and pre-operative serum PSA (prostate specific antigen) level.

Method and Material: 107 TURP (Trans Urethral Resection of Prostate) specimens were processed and studied. Histomorphological diagnosis is made. Correlation of final histological diagnosis with age and serum PSA level, applying one way ANOVA test, was determined.

Results: Out of 107 cases, the incidence of Low Grade PIN was 2 (1.9%), High Grade PIN was 1 (0.9%) and overall PIN was 3 (2.8%). The incidence of T1a was 4 (3.7%), of T1b was 2 (1.9%) and overall prostatic carcinoma was 6 (5.6%). Of these, there were 2 (33.3%) patients in the Gleason Grade 1 and 4 (66.7%) in the Gleason Grade 2. Statistically significant correlation of these premalignant and malignant lesions is demonstrated in comparison to age, whereas serum PSA level do not show any significant correlation.

Conclusion: Both, adenocarcinoma and PIN can be diagnosed on histopathological examination of TURP specimen.Probability of finding these premalignant lesions as well as incidental carcinoma in association with BPH increases with age.PSA levels are not significant indicator of presence of these lesions.

Keywords: Benign Prostatic Hyperplasia; Prostatic Intraepithelial Neoplasia; Prostatic Adenocarcinoma; Incidental Prostatic Carcinoma.

Introduction

Histological examination of the prostate must also include the description of some important aspects which may be present or associated with BPH and which may condition the progression of this disease. Occurrence of prostatic intraepithelial neoplasia (PIN) in transurethral resection of prostate specimens is relatively uncommon [1].

Incidental carcinoma is a incidental finding in prostate specimen resected for other causes like BPH. Prostate cancer is common, presenting clinically in 8% of men. On autopsy, up to 60% of 70-year-olds and 80% of 80-year-olds are found to have latent prostate cancer [2].

Incidence of prostatic disease, Nodular Hyperplasia (NH) and carcinoma increases with age. Transurethral resection of the prostate (TURP) targets the transitional

zone of the prostate. Prostate cancer isolated exclusively in the transitional zone (TZ) is uncommon, accounting for only 2–7% of all prostate cancers [3]. Several recent studies have reported that cancer arising from the TZ have a more favorable prognosis than tumors that arise in the peripheral zone (PZ) [4]. As a result, several groups argue that the TURP specimen may hold limited diagnostic value [5]. In the postprostate-specific antigen (PSA) testing era, incidental prostate cancer (ICP) on TURP remains common, occurring in 4.1–16.7% of TURP specimens [6]. Despite this prevalence, oncological outcomes have been poorly studied, with small series suggesting favorablesurvival [7].

Material and Methods

This was a cross sectional study which included TURP specimen of the clinically diagnosed BPH patients received from General surgery department of Index Medical College and Hospital. Prostatic chips obtained after trans- urethral resection from 107 patients operated for clinically diagnosed BPH.

Inclusion Criteria

Patient undergoing TURP for the clinical diagnosis of BPH.

Exclusion Criteria

We excluded patients who are positive for carcinoma in prostatic biopsy or clinically diagnosed as prostate carcinoma.

The prostatic chips obtained after TURP for the clinical diagnosis of BPH, sent for histopathological examination from department of general surgery, were collected and processed in the histopathology laboratory of Index Medical College, Hospital and Research Centre, Indore.

Standard handling of these specimens includes embedding and analyzing only part of larger specimen. The College of American Pathologists (CAP) recommend that specimens weighing ≤ 12 g should be examined in entirety. For specimens weighing > 12 g, the initial 12 g should be assessed with the addition of 2 g of tissue for every 10 g of specimen [8]. Intuitively, embedding the entire TURP specimen for histological examination will lead to a higher rate of identification of prostate cancer [9]. Despite this, literature suggests that partial assessment detects up to 90–100% of incidental cancer on TURP specimens [10].

Histomorphological diagnosis is made under microscopic examination. All the lesions were graded into non-neoplastic and neoplastic lesions. The cases of prostatic adenocarcinoma were graded using Gleason microscopic grading as well as staged according to TNM staging system.Comparison between different histological findings (groups) with respect to age and serum PSA level (from biochemistry laboratory).

Observations and Result

Four diagnostic categories were formed which included BPH, BPH with chronic prostatitis, PIN in association with BPH and incidental prostatic carcinoma.

The incidence of Low Grade PIN (LGPIN) was 2 (1.9%), High Grade PIN (HGPIN) was 1 (0.9%) and overall PIN was 3 (2.8%) out of total 107 cases of clinically diagnosed BPH.

The incidence of T1a was 4 (3.7%), of T1b was 2 (1.9%) and overall prostatic carcinoma was 6 (5.6%) out of total 107 cases of clinically diagnosed BPH.

Gleason grading was done for all 6 cases of prostatic carcinoma. Of these, there were 2 (33.3%) patients in the Gleason Grade 1 and 4 (66.7%) in the Gleason Grade 2.

Table 1 shows the comparison of mean age between the four groups. The mean age in BPH was 66.72±7.60 years, in BPH with chronic prostatitis is 64.49 ± 9.64 years, in PIN group was 78.67±11.37 years and in adenocarcinoma group it was 77.33±7.23 years. The mean age in PIN was highest while in the BPH with chronic prostatitis it was the least. There was a statistically significant difference in the mean age between the four groups (P<0.05).

Table 2 shows the comparison of mean PSA between the four groups. The mean PSA in BPH group was 5.96± 3.03 ng/ml, in BPH with chronic prostatitis is 6.02±2.14 ng/ml, in PIN group was 6.36±2.83 ng/ml and in adenocarcinoma group it was 8.04 ± 0.98 ng/ml. The mean PSA in adenocarcinoma was highest while in the BPH it

Table 1: Comparison of mean age in relation to groups

Groups	N	Age [Mean ± SD]	F Value	P Value
BPH	53	66.72 ± 7.60	5.99	0.001*
BPH with chronic prostatitis	45	64.49 ± 9.64		
PIN	3	78.67 ± 11.37		
Adenocarcinoma	6	77.33 ± 7.23		

One-way ANOVA applied. P value < 0.05 was taken as statistically significant
Abbreviations: BPH- Benign Prostatic Hyperplasia, PIN- Prostatic Intraepithelial Neoplasia, N- Number of cases, SD- Standard deviation

Table 2: Comparison of mean PSA (ng/ml) in relation to groups

Groups	N	PSA (ng/ml) [Mean ± SD]	F Value	P Value
BPH	53	5.96 ± 3.03	1.18	0.320, NS
BPH with chronic prostatitis	45	6.02 ± 2.14		
PIN	3	6.36 ± 2.83		
Adenocarcinoma	6	8.04 ± 0.98		

One-way ANOVA applied. P value < 0.05 was taken as statistically significant
Abbreviations: PSA- Prostate Specific Antigen, BPH- Benign Prostatic Hyperplasia, PIN- Prostatic Intraepithelial Neoplasia, N- Number of cases, SD- Standard deviation

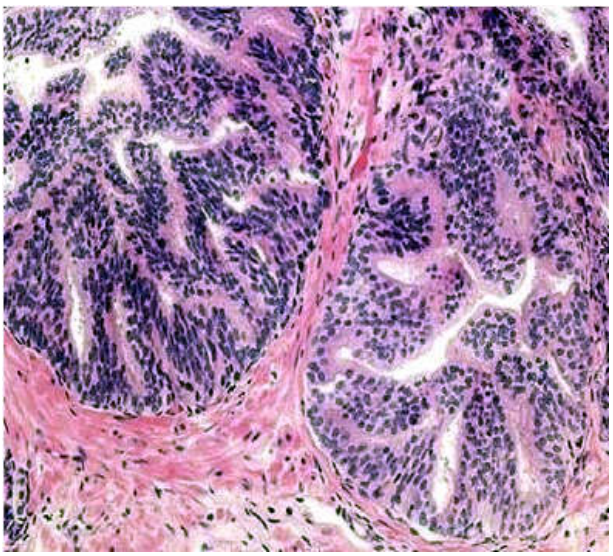

Fig. 1: HGPIN(High Grade Prostatic Intraepithelial Neoplasia); H & E, 40 X; in which epithelial cells show crowding, stratification, nucleomegaly, hyperchromatismandanisonucleosis. Fibromuscular sling is intact.

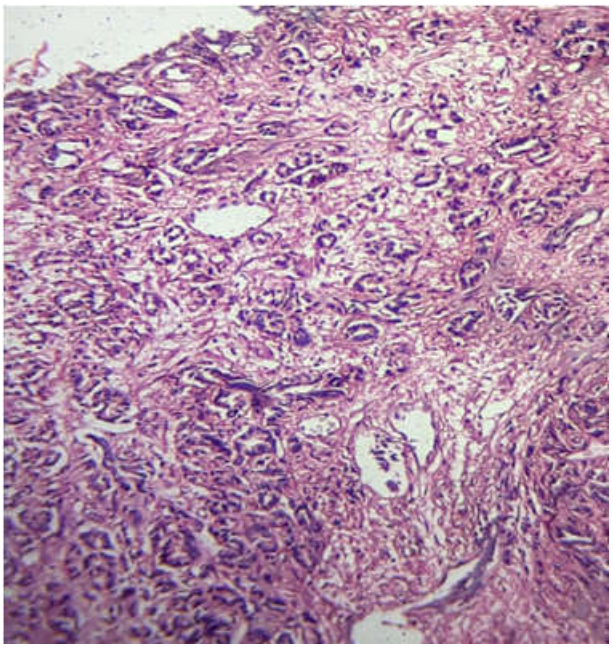

Fig. 2: Prostatic adenocarcinoma (Gleason Score 7); H & E, 10 X; Figure showing variably sized glands separated irregularly along with fused glandular mass with infiltrating edges.

was the least. There was a statistically not significant difference in the mean PSA between the four groups (P>0.05).

Discussion

The clinical significance of HGPIN as a pre-malignant lesion for prostate cancer has been well accepted; on the contrary, according to the consensus conference [11], LGPIN is regarded as having no diagnostic or therapeutic significance. McNeal and Bostwick underlined that PIN and prostate cancer are both age-associated lesions [12].

In our study, the incidence of LGPIN was 2 (1.9%), HGPIN was 1 (0.9%) and overall PIN was 3 (2.8%) out of 107 cases. Reddy et al.(2014) [13] found 8 cases of HGPIN with BPH out of 288 BPH cases, that is 2.7 %. Di Silverio et. al.(2003) [14] found that PIN was present in 2.1% of all BPH cases with similar distribution for LGPIN (1.1%) and HGPIN (1.0%).

In present study, the incidence of T1a prostatic carcinoma was 4 (3.7%), of T1b prostatic carcinoma was 2 (1.9%) and overall prostatic carcinoma was 6 (5.6%) out of 107 clinically diagnosed BPH cases. These findings are similar to the findings in other studies by, Dellavedova et. al.(2010) [15] in their study, presented 7 cases of prostate cancer detected in 100 patients who underwent bipolar transurethral resection (TUR) of the prostate due to regular indications. Jones et. al.(2009) [16] conducted a study,in which comparison was made of transurethral resection of prostate (TURP) cohorts in the pre-PSA era (1986–1987) and the PSA era (1994–2000), excluding patients with known PCa, found that malignancy diagnosed at the time of TURP decreased from 14.9 to 5.2% of patients in the pre-PSA and PSA eras, respectively and also stage T1a decreased from 4.4 to 2.4% and Stage T1b decreased from 10.5 to 2.8% of patients in the pre-PSA and PSA eras, respectively. Lee et. al.(2013) [17] in their study, examined 156 patients of incidental prostatic carcinoma, out of which 97 (62.2%) had T1a and 59 (37.8%) had T1b supports our finding of incidence of T1a carcinoma, constituting 66.7%, to be more than T1b carcinoma (33.3%). Zigeuner et. al. (2003) [6] in their study found that the rate of incidental prostate cancer in patients with both negative age-specific PSA levels and negative

DRE findings was 6.4% (72 of 1127). Di Silverio et . al. (2003) [14] found incidental carcinoma in 5.5% of cases, with a higher percentage for T1a (4.7%) as compared to T1b (0.8%) carcinomas, and revealed that in T1a tumors, the distribution of Gleason score was <6 in 89.7% and 6 in 10.3% of cases. None of T1a carcinomas showed a Gleason score of 7 or more. In T1b cases, the distribution of Gleason score was <6 in 37.5%, 6 in 28.1% and 7 in 34.4% of cases. Where in our study, out of 6 diagnosed carcinoma, 4(2 T1a and 2 T1b) are Gleason grade 2 (Gleason score 5-7) and 2 (all T1a) are Gleason grade 1 (Gleason score 2-4), however no significant correlation was found between TNM stage and Gleason grade.

In this study, association of different histological findings with age was analyzed and found that the mean age in BPH was 66.72±7.60 years, in BPH with chronic prostatitis is 64.49±9.64 years, in PIN group was 78.67± 11.37 years and in adenocarcinoma group it was 77.33±7.23 years. There was a statistically significant difference in the mean age between the four groups (P<0.05). Lee et al.(2013)[17], in their study, retrospectively reviewed the records of 156 incidental prostate cancer patients between 2001 and 2012 and found that the mean age of incidental carcinoma to be 69.5±6.4. Dellavedova et. al.(2010) [15], presented 7 cases of prostate cancer detected in 100 patients who underwent bipolar transurethral resection (TUR) of the prostate due to regular indications with mean age of 69 years. Jones et . al. (2009) [16] in their study revealed that average age at time of operation was 72.6 years in the pre-PSA era and 72.9 years in the PSA era in cases of incidental prostatic carcinoma. Di Silverioet al.(2003)[14] in their study, regarding PIN, the distribution in the different decades of age significantly varied (p=0.030); for HGPIN, there was a significant trend to increase with age decades and also, a significant difference in the distribution of incidental carcinoma (T1a, T1b) in the different decades of age was found (p=0.001), and in particular, in regards to both T1a and T1b tumors, there was a trend to increase from group(50-59years) to group(80- 89 years).

In our study, the mean PSA in BPH group was 5.96±3.03 ng/ml, in BPH with chronic prostatitis is 6.02±2.14 ng/ml, in PIN group was 6.36±2.83 ng/ml and in adenocarcinoma group it was 8.04±0.98 ng/ml. The mean PSA in adenocarcinoma was highest while in the BPH it was the least. There was statistically no significant difference in the mean PSA between the four groups (P>0.05). Lee et al.(2013) [17] found after studying 156 cases of incidental carcinoma that the average PSA before TURP was 4.57±4.24 ng/mL and 1.43±1.66 ng/mL after TURP. Dellavedova et al. (2010) [15] studied 7 cases of incidental carcinoma, and found mean serum PSA to be 6.4ng/ml. Jones et. al.(2009) [16] in their study showed that the median PSA of patients who were found to have incidental prostate cancer during the PSA era was 6.9 for those with stage T1a and 4.7 for those for stage T1b (P=0.79). Di Silverio et .al. (2003) [14] found the mean PSA value for LGPIN to be 4.6±1.3ng/ml, for HGPIN to be5.9±2.3ng/ml, for T1a incidental cancer to be 4.9±2.1ng/ml, for T1b incidental cancer to be 7.9±2.2ng/ml in cases operated for BPH.

Conclusion

Both, adenocarcinoma and PIN can be diagnosed on histopathological examination of TURP specimen. One should *examine carefully* for the presence of these lesions. Probability of finding these premalignant lesions as well as incidental carcinoma in association with BPH increases with age. PSA levels are not significant indicator of presence of these lesions.

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