

Morphological Spectrum of Prostatic Lesions - A Clinicopathological Study

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Abstract

Background and objectives : Study of prostatic lesions has gained more importance because development of prostatic hyperplasia is an almost universal phenomenon in aging men. Inflammatory conditions need correct diagnosis as they can be treated with antibiotics. Prostatic carcinoma is the second most common cause of death in men over age of 55 years.

Methods : The study included prostatic tissue specimens received in the pathology laboratory at Kempegowda Institute of Medical Sciences and Hospital, Bangalore from December 2003 to December 2005. A total of 150 specimens were studied. They were graded into benign, inflammatory conditions and malignant lesions. Gleason's microscopic grading was used to grade all the prostatic adenocarcinoma cases. Serum prostate specific antigen (PSA) levels were correlated in all the cases.

Results : There were 134 transurethral resections of prostate (TURP), 12 needle biopsies and 4 prostatectomy specimens. Most of the patients were in sixth and seventh decade. Lesions encountered were nodular hyperplasia (NH) / prostatitis 90%, high grade prostatic intraepithelial lesion (HGPIN) 0.7% low grade prostatic intraepithelial lesion (LGPIN) and 9.3% malignant. Nodular hyperplasia was the common lesion encountered. Associated lesions like prostatitis basal cell hyperplasia, clear cell cribriform hyperplasia, transitional metaplasia, granulomatous prostatitis, abscesses were encountered. Among the malignant lesions, adenocarcinoma (Gleason's score 7) was the common lesion seen in seventh decade. An interesting case of primary squamous cell carcinoma was encountered. One of the case sent as metastatic transitional cell carcinoma from bladder was confirmed histologically. Serum prostate specific antigen (PSA) levels were elevated in few cases of benign lesions due to associated lesions like prostatitis, abscesses and granulomatous prostatitis. Many of the malignant cases showed very high levels of PSA.

Keywords : Adenocarcinoma of prostate; Gleason's score; prostate specific antigen.

Introduction

Prostate gland occupies center stage in the lives of many elderly males. Because of its location at bladder neck, enlargement of the gland leads to problems related to urinary obstruction[1]. Incidence of prostatic disease, NH and carcinoma increases with age. Recently there has been a significant advance in understanding of various prostatic diseases.

Prostatitis, NH and tumors are the three important lesions to be studied in detail as they are frequently encountered. Diagnosis of prostatitis is very necessary as they can be successfully treated with antibiotics. NH describes a hyper plastic process of stromal and epithelial elements of prostate. It is an extremely common problem in elderly men over the age 50[1].

Prostatic carcinoma is more common in India compared to other Asian Countries[2]. It is the 5th cause of cancer in men and 4th in cancer mortality in India. At some time in their lives approximately one in 22 Indian males will be struck by prostatic carcinoma and its incidence is increasing by 3.5% every year[3]. Hereditary factors have a role[4]. Diet rich in animal fats, red meat and diet poor in fruits, vegetables are the likely culprit in prostatic carcinoma [5]. Low levels of dietary selenium, vitamin E and vitamin D also play a role [6]. Studies also reveal that there is no definite role of sexual activity, smoking, height, weight and alcohol consumption [7].

Although nodular hyperplasia can almost be considered as an aging process, the histological variations like different types of hyperplasias, low grade

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prostatic intraepithelial neoplasia (LGPIN) and high grade prostatic intraepithelial neoplasia (HGPIN) merits discussion.

Prostatic carcinoma also has to be given importance as its incidence is increasing owing to the westernization in Asian countries including India. This study comprises description of incidence of various lesions of prostate encountered, associated clinical manifestations, morphological changes and also serum PSA level correlations. It is all the more necessary to study prostatic diseases in the present situation as their incidence keeps growing due to extended male longevity past the 60s [3].

Materials and Methods

The present study included prostatic tissue specimen received in the pathology laboratory at Kempegowda Institute of Medical Sciences. Brief clinical data were noted from the case records, which included the age presenting symptoms, serum PSA levels and clinical diagnosis.

The specimens thus obtained were fixed in 10% formalin after detailed and careful examination. In case of TURP, approximately 5gm of tissue was processed in one cassette and embedded. The entire tissue was processed in case of needle biopsy and in cases of prostatectomy representative bits were processed. Then sections 4 to 6 microns thick were prepared. These were stained routinely with hematoxylin and eosin.

Other special stains like Alcian blue pH 1, periodic acid schiff (PAS) and ZiehlNeelson were performed wherever necessary. The procedure followed for tissue processing and staining technique are those given in "Cellular Pathology technique" by CFA Culling[8]. All the lesions were graded into non-neoplastic and neoplastic lesions. The cases of prostatic adenocarcinoma were graded using Gleason microscopic grading.

The clinical and histological data so obtained were analyzed and compared with another similar studies.

Statistical methods

Chi-square and Fisher exact test have been used to test the proportions in association of lesions and Serum PSA values. The data was analyzed using SPSS 11.0 and Systat 8.0 .

Results

Benign lesions were common in the age group of 60-69 years while malignant lesions were common in the age group 70-79 years (Table 1). However, when

benign and malignant lesions were compared, benign cases commonly occurred in the age of 40-59 years and malignant lesions peaked in 70-79 years.

Frequency was the most common symptom in benign lesions followed by difficulty in voiding, acute retention and dysuria (Table 2). Malignant lesions had common symptoms of dysuria, incomplete voiding and frequency. However when both lesions were compared poor stream was positively associated with benign lesions and incomplete voiding, hematuria and dysuria were significantly associated with malignant lesions.

In benign lesions serum PSA was normal in 75 cases (55.1%). Modest elevation [4.1-10 ng/ml] was seen in 36 cases (26.4%) and marked elevation [>10 ng/ml] in 25 cases (18.3%) due to associated conditions like chronic prostatitis, granulomatous prostatitis and abscesses. In malignant prostatic lesion, 8 cases (57.1%) showed marked elevation in serum PSA levels (>20 ng/ml)(Table 3).

Gleason's microscopic grading was adopted for grading prostatic adenocarcinoma in which the commonest Gleason score was score 7 (58.3%), followed by score 8 (25%) and score 9 (16.7%)(Table 4). Low-grade lesions were not encountered probably because these lesions are usually asymptomatic. Final histopathological diagnosis in the cases studied included 123 cases of Nodular Hyperplasia (98 NH without Prostatitis & 25 NH with Prostatitis), 13 cases of PIN (12 LGPIN & 1 HGPIN), 12 cases of adenocarcinoma & one case each of Metastatic Transitional cell carcinoma from bladder & Squamous cell carcinoma.(Table 5).The present study was carried out from December 2003 to December 2005, at the Kempegowda institute of Medical Sciences, Bangalore.

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Table 1. Age incidence of the various prostatic lesions

Age (yrs)	Benign n (%)	Malignant n(%)	Total n(%)	p value
30 - 39	-	-	-	-
40 - 49	4 (2.94%)	-	4 (2.67%)	p>0.05
50 - 59	19 (13.97%)	1 (7.14%)	20 (13.33%)	0.694
60 - 69	55 (40.44%)	6 (42.86%)	61 (40.67%)	0.861
70 - 79	49 (36.03%)	7 (50.00%)	56 (37.33%)	0.303
80 - 89	9 (6.62%)	-	9 (6.00%)	p>0.05
Total	136 (100.00%)	14 (100.00%)	150 (100.00%)	-
Inference	Malignant cases are more commonly seen in the age group of 70-79 years with p=0.303 and benign cases are more common in the age group of 40-59 years with p=0.470.			

Table 2. Clinical presentation of prostatic lesions

Clinicals Symptoms	Benign (n=136)	Malignant (n=14)	Total (n=150)	p value
1. Frequency	50 (36.5)	5 (38.5)	55 (36.67)	0.323
2. Nocturia	10 (7.3)	2 (15.4)	12 (8.00)	0.278
3. Urgency	7 (5.1)	-	7 (4.67)	p>0.05
4. Difficulty in voiding	39 (28.5)	3 (23.1)	42 (28.00)	p>0.05
5. Straining	3 (2.2)	-	3 (20.00)	p>0.05
6. Poor stream	15 (10.9)	-	15 (10.00)	0.364
7. Hesitancy	2 (1.5)	-	2 (1.33)	p>0.05
8. Incomplete voiding	19 (13.9)	5 (38.5)	24 (16.00)	0.036*
9. Hematuria	1 (0.7)	2 (15.4)	3 (2.00)	0.020*
10. Acute retention	31 (22.6)	2 (15.4)	33 (22.00)	0.734
11. Dysuria	21 (15.3)	5 (38.5)	26 (17.33)	0.050*
Inference	Incomplete voiding, hematuria, dysuria are significantly associated with the malignant lesions with p<0.05, poor stream is positively associated with benign lesions with p=0.364.			

Figures in parenthesis are percentages

* Significance at 5%

Table 3. Serum PSA levels in the cases studied

PSA(ng/ml)	Benign	Malignant
0-4	75	2
4.1-8	25	0
8.1-12	11	3
12.1-15	1	1
16.1-20	5	0
>20.1	19	8
Total	136	14
Inference	PSA values with >20.1 are 8.21 times more likely to be malignant with p=0.001	

Table 4. Incidence of carcinoma with reference to Gleason's score (maximum Score 10)

Gleason's Score	No. of Cases
2	-
3	-
4	-
5	-
6	-
7	7 (58.3%)
8	3 (25%)
9	2 (16.7%)
10	-
Total	12 (100%)

Discussion

Enlargement of prostate is an age related process and incidence increases with increasing age beginning in the forties. The incidence of NH increases from an average of 23 to 88% by the ninth decade [9]. Most patients over the age of 50 years will have histological evidence of NH and many will suffer symptoms from urethral compression.

Data indicate that on microscopic examination both epithelium and stroma are involved in varying degrees and predominant pattern is fibroadenomatous hyperplasia.

In the present study adenofibromyomatous hyperplasia were seen in 136 cases where hyperplasia of both epithelial and stromal components were seen.

Table 5. Final histopathological diagnosis in the cases

1) NH a) Without Prostatitis b) With Prostatitis	98(65.3%) 25(16.6%)
2) PIN a) LGPIN b) HGPIN	12(8.0%) 1 (0.7%)
3) Adenocarcinoma	12(8%)
4) Metastatic TCC (from Urinary Bladder)	1(0.7%)
5) Squamous Cell Carcinoma	1(0.7%)

According to study by Bostwick et al. NH is composed of varying proportion of epithelium and stroma. The most common nodules reported in their study was adenofibromyomatous nodules which contained all elements [10].

Prostatic intraepithelial neoplasia (PIN)

In the present study out of 150 specimens examined, 19 cases showed PIN. 12 cases were LGPIN which was associated with NH and 7 cases showed HGPIN out of which 1 was associated with NH and the rest 6 were associated with prostatic carcinoma. LGPIN was characterized by epithelial crowding and stratification with anisonucleosis but no prominent nucleoli was observed (Figure 1).

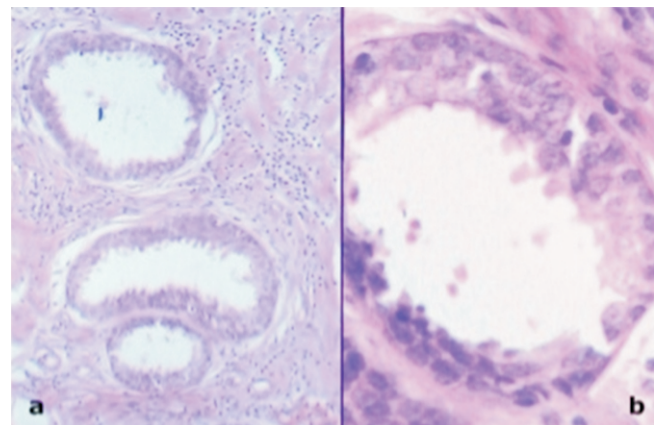


Figure 1. Low grade PIN showing epithelial crowding and stratification with anisonucleosis (a) H&E, 100X(b) H&E, 400X

Prostatic Carcinoma

In the present study, peak incidence of both PIN and prostatic carcinoma was seen in age group of 70-79 yrs. It has been observed that PIN occur at least a decade earlier compared to prostatic carcinoma. But in present

study no such age difference was noted. Many recent studies show a higher incidence of prostatic carcinoma in the age group of 61-70 years. However in studies of Moore and Baron, the peak incidence was seen in age group of 51-60 years. This may indicate change in trend of prostatic carcinoma.

Present study showed 90.7% of NH and 9.3% prostatic carcinoma. Anna Pacelli and David G. Bostwick reported incidence of 81.7% of NH and 18.3% adenocarcinoma [11]. NH is a common cause of serum PSA elevation and accounts for 60-70% of cases. Studies of patients with histologically confirmed NH have shown that 21-86% have elevated serum PSA levels. The degree of elevation is modest (4.1-10ng/ml)[12]. In the present study 36 cases had modest elevation of PSA levels and remaining 25 cases the degree of elevation was severe with 19 cases having levels more than 20.1 ng/ml. This is because these cases of NH were associated with prostatitis, abscesses and granulomatous prostatitis (figures 2, 3, 4). Serum levels of PSA were frequently elevated in patients with PIN ranging from 0.3 to 22.3 mg/ml (mean 4.0)[13]. In the present study, they showed normal levels (<4 ng/ml)

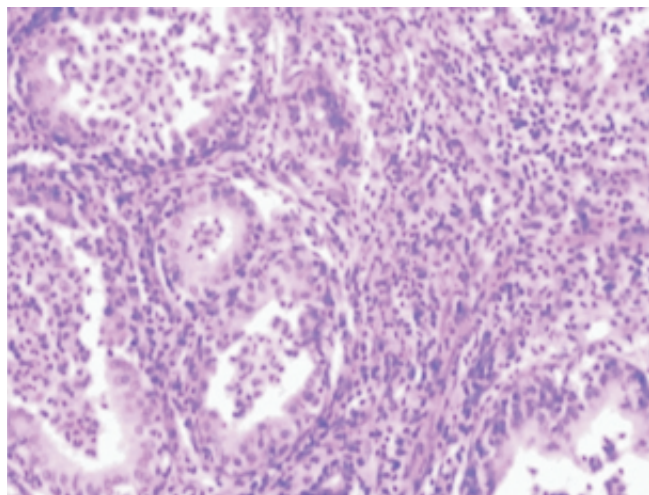


Figure 2. Prostatic abscess showing sheets of neutrophils in and around the acini (H&E, 100x)

PIN accounted for 8.6% (13 cases) with a peak incidence in age group of 0-79 years. LGPIN accounted for 8% (12 cases) and HGPIN accounted for 0.6% (1 case).

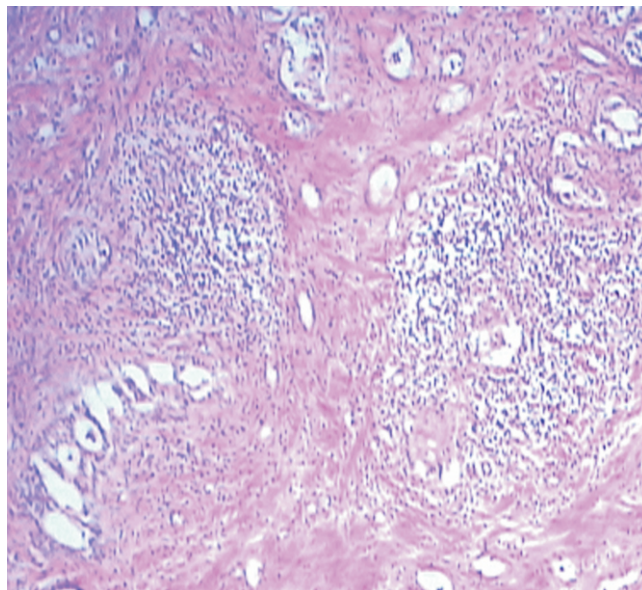


Figure 3. Chronic prostatitis showing infiltration of lymphocytes, plasmacells and histiocytes in the stroma (H&E, 100X)

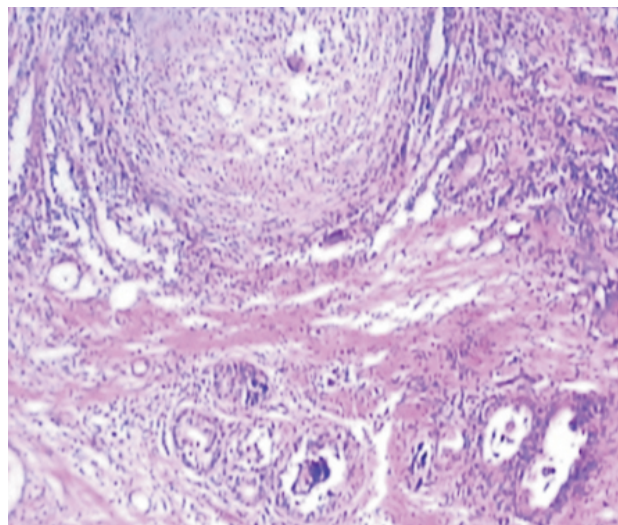


Figure 4. Granulomatous prostatitis showing well formed epithelioid granuloma with a giant cell (H&E, 40x)

LGPIN were reported in view of complete description of histologic variants. Incidence of isolated HGPIN was low because most of the specimens studied included TURP, which is from transition zone, and HGPIN is common in peripheral zone. However HGPIN(figure 05) was noted in adjacent prostatic tissue in 6 cases (50%) of prostatic adenocarcinoma out of 12 cases of adenocarcinoma. Malignant lesions showed a peak incidence in the age group of 60-69 years. In benign lesions serum PSA was normal in 75

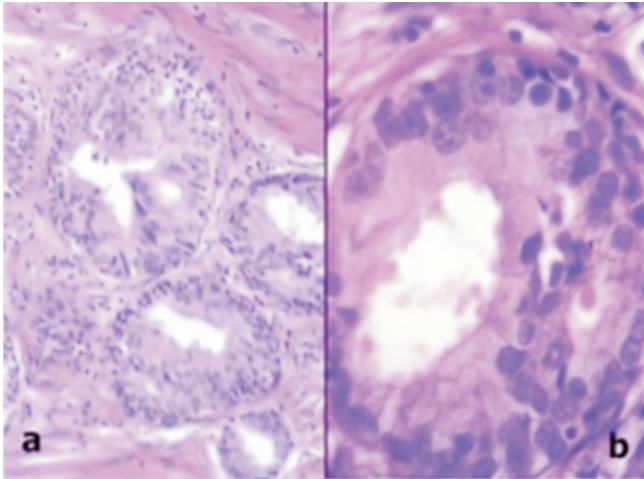


Figure 5. High grade PIN showing pronounced epithelial crowding, stratification, nuclear enlargement with prominent nucleoli and intact basement membrane.(a) H&E, 100X(b) H&E,400X

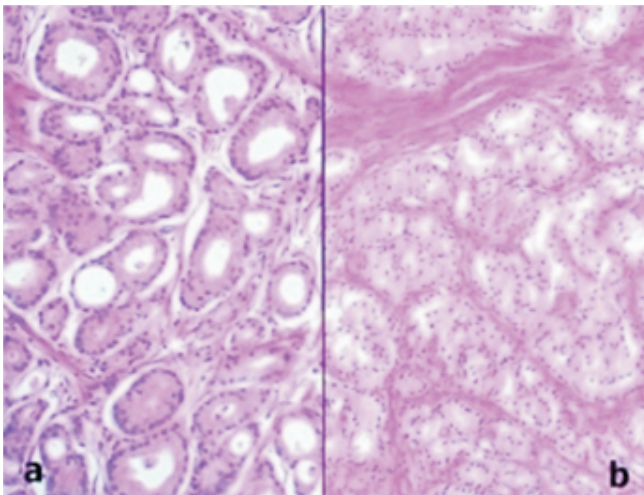


Figure 6. Prostatic adenocarcinoma, Gleason's score 3+4=7/10 (a) pattern 3 showing closely packed single glands (b) pattern 4 showing fused glandular pattern (H&E,100X)

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