Original Research Article

Correlation of various histopathological lesions of prostate with serum prostate specific antigen and gleason grading

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ABSTRACT

Introduction: Present study was conducted to determine the age distribution of patients with prostatic lesions, prevalence of distribution of various prostatic lesions and to study correlation of histopathological types of prostatic lesions with prostate specific antigen (PSA).

Materials and Methods: A total 246 prostatic needle biopsies from patients of all age groups were included in the study. After studying the histopathological features, the diagnosis of various types of prostatic lesions was made and Gleason's scoring was done in cases of prostatic carcinoma. Subsequently, a correlation was made between the histopathological diagnosis and serum PSA level.

Results: The Mean±Sd of age is 69.7±9.9 years. In pure inflammatory lesions, LGPIN, HGPIN, BPH, and BPH with prostatitis majority had PSA level <4ng/ml. in malignant cases majority had PSA level above 20 ng/ml. Majority of 65 (80.25%) cases of carcinoma prostate were found poorly differentiated (G3-4) followed by 14 (17.28%) cases were moderately differentiated (G2) and least 2 (2.3%) cases were diagnosed well differentiated (G1). There were 0 cases whose Grade cannot be assessed (Gx).

Conclusion: Histopathological diagnosis and grading plays an important role in the management of prostatic cancer. For satisfactory management of patient, a high degree of the awareness of the advances along with team approach has become imperative.

1. Introduction

Prostatic carcinoma is an important growing health problem, presenting a challenge to urologists, radiologists and pathologist.[1,2] Prostate cancer is the leading cause of new cancer in men and is second only to lung cancer as a leading cause of cancer-related deaths in men.[3]

Worldwide benign prostatic hyperplasia (BPH) affects 210 million males and is common over the age of 50 years.[4,5] Carcinoma of the prostate is most common non-skin cancer in the west and the second leading cause of cancer death among men.[6,7] In India, carcinoma of prostate occupies 2nd to 10th rank among cancers in men, in various metro cities as per national cancer registry.[8,9]

Several factors, including age, race, family history, hormone levels, and environmental influences are suspected to play a role in pathogenesis. Because of the location of prostate gland at bladder neck, enlargement of the gland leads to problems related to urinary obstruction. The incidence of prostatic diseases, benign prostatic hyperplasia, and carcinoma increases with age.[4] Benign prostate hyperplasia, prostate carcinoma and prostatitis are three pathologic processes which frequently affect the prostate gland. It is extremely common problem in elderly men over the age of 50 years.[4]

PSA is the most important and clinically useful biochemical marker of the prostate because it is produced by and is specific for prostatic tissue.[10] Normal levels of PSA are usually less than 4 ng/ml, but they vary according to the age of the patient.[11] PSA levels less than 4 ng/ml in men of

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60 years or less and levels less than 6.5 ng/ml in men aged 60-80 years are normal. PSA is elevated by any change that disrupts the normal architecture of the prostate which allows diffusion of protease into the microvascular circulation.

Gleason grading is one of the most powerful predictors of biological behavior and influential factors used in determining treatment.[4]

The present study includes description of incidence of various lesions of prostate, their clinical manifestations, serum PSA level, classification, and grading of prostate tumors. Thus, present study was undertaken to evaluate Prostatic biopsies by the Pathology Department in SP Medical College and A.G. of Hospitals and assess their incidence, prevalence and study of the various histological types and their correlation with PSA.

2. Materials and Methods

The present study was conducted in Department of Pathology, SP medical college, Bikaner. Study consisted of prostate needle biopsies obtained from patients clinically diagnosed as nodular hyperplasia of prostate and carcinoma of prostate who attended the OPD of Surgery and Urosurgery Department of PBM Hospital, Bikaner.

A total 246 prostatic needle biopsies from patients of all age groups were included in the study. The section was examined for histomorphological characters of prostate like stromal and glandular proliferation, presence of myoepithelial cell layer in nodular hyperplasia of prostate and irregularity of glandular contour, nuclear enlargement, hyperchromasia, and most important prominent nucleoli in carcinoma prostate.

After studying the histopathological features, the diagnosis of various types of prostatic lesions was made and Gleason's scoring was done in cases of prostatic carcinoma. Subsequently, a correlation was made between the histopathological diagnosis and serum PSA level.

3. Results

We received total 246 prostate needle biopsies in our Department of Pathology, SP Medical College, Bikaner.

The Mean age is 69.7±9.9 years with majority of patients (36.18%) were in age group 61-70 years followed by 30.49% in age group 71-80 years. The most common type of lesion was benign (63.82%%) followed by 33.33% malignant lesions and 2.85% cases were pure inflammatory lesion.

Out of total pure inflammatory lesions cases, 1 case (14.3%) had acute, 3 (57.1%) chronic and 2 (28.6%) granulomatous lesions. From total benign lesion, 15 (11.62%) cases had BPH with prostatitis, 114 (88.38%) had BPH without prostatitis. From PIN 11 (39.28%) cases had LGPIN and 17 (60.72%) cases of HGPIN. Out of total Malignant lesions, 81 (98.78%) cases had adenocarcinoma

and 1 (1.22%) had Metastatic TCC (Table 1).

Table 1: Histopathological diagnosis in case studies

Pure inflammatory (n=6)		
	No.	%
Acute	1	14.3
chronic	4	57.1
Granulomatous	2	28.6
Total	7	100
Benign (n=129)		
BPH With Prostatitis	15	11.62
BPH Without Prostatitis	114	88.38
Total	129	100
PIN (N=28)		
LGPIN	11	39.28
HGPIN	17	60.72
Total	28	100
Malignant (n=82)		
Adenocarcinoma	81	98.78
Metastatic TCC	1	1.22
Total	82	100

Table 2 show PSA Level in Various Prostatic Lesions. In pure inflammatory lesions, LGPIN, HGPIN, BPH, and BPH with prostatitis majority had PSA level <4ng/ml. in malignant cases majority had PSA level above 20 ng/ml.

Figure 1 shows Distribution of different type of lesions in different age group. We found that majority of Pure inflammatory lesion were in age group ≤50 years. BPH, BPH with prostatitis, LGPIN, HGPIN lesion were most common in age group 61-70 years and malignancy was most prevalent in age group above 70 years. Figure 2 shows among malignant cases according to Gleason Score. Majority of patients had Gleason score of 6-8 with 5 cases had a Gleason score of 9.
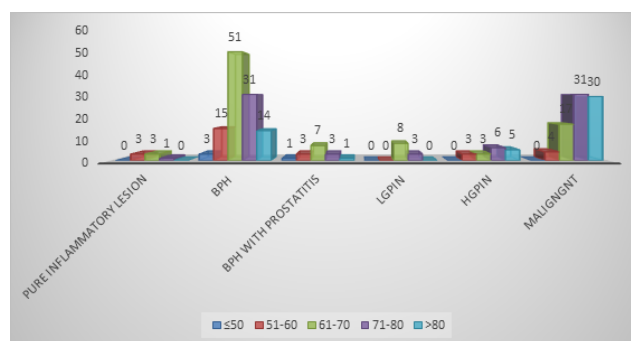

Fig. 1: Distribution of different type of lesions in different age group

Figure 3 shows Evaluation of histological grade in malignant cases. Here, majority of 65 (80.25%) cases of carcinoma prostate were found poorly differentiated (G3-4) followed by 14 (17.28%) cases were moderately differentiated (G2) and least 2 (2.3%) cases were diagnosed

Table 2: PSA level in various prostatic lesions

PSA Level (ng/ml)	Pure Inflammatory Lesion	BPH	BPH with prostatitis	LGPIN	HGPIN	Malignant
<4	3	65	11	9	11	0
4.1-10.0	0	7	4	2	5	0
10.1-20.0	4	27	0	0	1	0
20.1-40.0	0	11	0	0	0	28
40.1-60.0	0	3	0	0	0	19
60.1-80.0	0	1	0	0	0	13
80.1-100.0	0	0	00	0	0	7
>100.0	0	0	0	0	0	15
Total	7	114	15	11	17	82

Chi Square Value=37.8; d.f.=1; p=0.0001
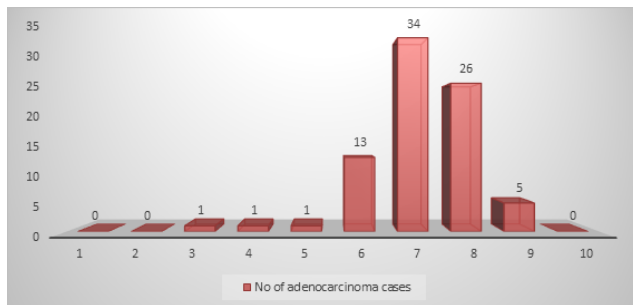
Fig. 2: Distribution of malignant cases according to gleason score
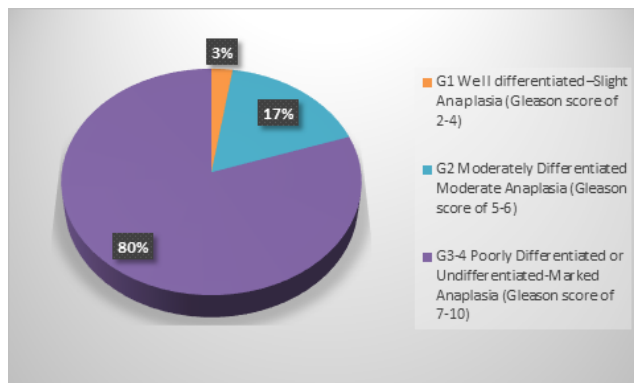
Fig. 3: Evaluation of histological grade in case study

well differentiated (G1). There were 0 cases whose Grade cannot be assessed (Gx).

4. Discussion

Prostatism is common in the geriatric age group. Benign prostatic hyperplasia and carcinoma of the prostate are increasingly frequent with advancing age and are uncommon before the age of 40 years.

The Mean age is 69.7±9.9 years with majority of patients (36.18%) were in age group 61-70 years followed by 30.49% in age group 71-80 years. In consistent with this Khant et al. found 66.9 ± 9.4 years.[12] Jayapradeep et al. found that maximum number of patients were in the age group of 60-70 years consisting of 90 cases. Above the age of 70 years, there were 48 cases and below 60 years 32 cases were present. The mean age of the patients was 65.58 years.[13] Hirachand et al found that maximum number of cases (n=47; 36.72%) were in the age group of 61-70 years followed by 71-80 years age group (n=43; 33.5%). Only 2 cases (1.56%) were observed younger than 50 years of age.[14] Mor et al found that Maximum incidence was found in the age group of 50-60 years. Mean age of presentation was 64.46.[15]

In our study The most common type of lesion was benign (52.43%) followed by 33.33% malignant lesions, 11.38% had PIN and 2.85% cases were pure inflammatory lesion. In concordance with this Khant et al. found that 69 (62.72%) cases showed benign lesions and 41 (37.2%) were malignant.[12] Jayapradeep et al. found 125 (73.5%) cases of NPH, 31 (18.2%) cases of prostatic adenocarcinoma.[13] Maru et al. found 81.5% Benign and 6.87% adenocarcinoma.[16] Hirachand et al. found 79.69% cases of benign and 20.31% cases of malignant type.[14]

Present study shows that majority of Pure inflammatory lesion were in age group ≤50 years. BPH, BPH with prostatitis, LGPIN, HGPIN lesion were most common in age group 61-70 years and malignancy was most prevalent in age group above 70 years. Hirachand et al. found that Benign prostatic hyperplasia (BPH) was the most common histological lesion encountered (n=95; 74.22%) with maximum incidence seen in 61-70 age group (35 cases) followed by 71-80 age group (30 cases). In malignant type of lesions maximum incidence seen in 71-80 age group (5 cases) followed by 81-90 age group (5 cases).[14] Jayapradeep et al found that among 125 cases of NPH, maximum number of cases (71) were in the age group of 60-70 years. Maximum incidence of prostatic adenocarcinoma (15) was in the age group of 70-80 years.[13] Khant et al found maximum number of benign cases 40 (36.36%) were 61–70 age group followed by 18 (16.36%) cases in 50–60 age groups. In malignant lesions maximum number of cases 22 (20%) were 61–70 age group followed by 15 (13.63%)

cases in >70 years age groups.[12]

In our study out of total pure inflammatory lesions cases, 1 case (14.3%) had acute, 3 (57.1%) chronic and 2 (28.6%) granulomatous lesions. From total benign lesion, 15 (11.62%) cases had BPH with prostatitis, 114 (88.38%) had BPH without prostatitis and 11 (39.28%) cases had LGPIN and 17 (60.72%) cases of HGPIN. Out of total Malignant lesions, 81 (98.78%) cases had adenocarcinoma and 1 (1.22%) had Metastatic TCC. In concordance with this Wadgaonkar et al found that 60% cases had BPH without prostatitis and 22.5% had BPH with prostatitis, 13.75% cases had adenocarcinoma and 1.25% had Transitional cell carcinoma.[17] Sharma et al. found 86.4% Chronic prostatitis followed by 9.8% Acute prostatitis and 3.7% Granulomatous prostatitis.[18] In our study 50% had chronic prostatitis followed by 33.3% Granulomatous prostatitis and 16.7% Acute prostatitis. These findings are also similar to the studies of Kasliwal N, Mathi A et al. and Puttaswamy K et al.[6,19,20]

In our study PSA Level in Various Prostatic Lesions. In pure inflammatory lesions, LGPIN, HGPIN, BPH, and BPH with prostatitis majority had PSA level <4ng/ml. in malignant cases majority had PSA level above 20 ng/ml. In consistent with this study by Study by Khant et al found that in benign lesion 63 cases had serum PSA level <4-10 ng/ml, 12 cases had serum PSA level >10.1-20 ng/ml and 4 cases had serum PSA level >20.1 ng/ml. In cases of malignant lesion 10 cases had serum PSA level <4-10 ng/ml, 14 cases had serum PSA level >10.1-20 ng/ml and 17 cases had serum PSA level >20.1 ng/ml[12].

Koteswari and Sudhakar[7] found 25% malignant cases having PSA level 0-≤4 ng/ml, 75% malignant cases having PSA level >10 ng/ml. Nadam et al[21] found 5.88% malignant cases having PSA level 0-≤4 ng/ml, 82.3% malignant cases having PSA level >10 ng/ml and 11.76% malignant cases having PSA level 4.1-10 ng/ml. similarly Nadam et al[21] found 51.58% benign cases having PSA level 0-≤4 ng/ml, 5.26% benign cases having PSA level >10 ng/ml and 43.16% benign cases having PSA level 4.1-10 ng/ml. Sladana Zivkovic et al[22] found 2.50% malignant cases having PSA level 0-≤4 ng/ml, 70% malignant cases having PSA level >10 ng/ml and 27.50% malignant cases having PSA level 4.1-10 ng/ml. Khant et al study found marked raised serum PSA level were found in 75.60% which was comparable with other studies. This is an interesting finding which shows that patients with markedly elevated serum PSA levels are more likely to harbor adenocarcinoma in their biopsies than benign changes.[12] Umbehr MH et al. and Kiehl R et al. in their studies concluded that BPH and prostatitis is associated with high serum PSA, when glandular epithelium is disrupted.[23,24] On the other hand, Papsidero LD et al. suggested that elevation of PSA is due to unknown substances released by epithelial cells in association with the inflammatory processes surrounding the affected area.[25]

In our study gleason score 7 (34 cases) was most commonest score was found followed by GS 8 (26 cases), and GS 6 (13 cases). In consistent with this Deshmukh et al found Gleason score 9 was the commonest score with 33.3% cases followed by GS 7 and GS 8 was present in 27.7% cases and gleason score 6 and 10 was present in 5.56% cases each.[26] Nwafor et al found Gleason score (GS) 7 was the most common score and was seen in 32.3% of carcinoma patients cases while 17.7% of carcinoma patients cases had GS 9 and 14.5% had GS 6. The least score recorded was GS 3, which was seen in 1.6% of cases.[27] The Gleason grading system, based on architectural features of prostate cancer cells, is the most widely used histological grading method for prostatic adenocarcinoma. The GS closely correlates with clinical behaviour and provides an important index of prognosis. Furthermore, this score is one of the key determinants in treatment decision making, together with stage, age, and PSA. It is the only grading system that recognizes the histologic heterogeneity of tumor present within a single prostate specimen by assigning grades to the primary and secondary patterns and combining this grade into the score (scored as 2-10). Though reproducible, across different institutions, stage, and grade depend on the subjective assessment of the investigator's. Studies have shown that patients with a pathological GS of ≤6 have an excellent progress-free survival, which can be up to 90%. However, men with a GS ≥7 adenocarcinoma have a 29-43% risk of death from prostate cancer.[27]

In our study majority of 65 (80.25%) cases of carcinoma prostate were found poorly differentiated (G3-4) followed by 14 (17.28%) cases were moderately differentiated (G2) and least 2 (2.3%) cases were diagnosed well differentiated (G1). There were 0 cases whose Grade cannot be assessed (Gx). In concordance with this Nwafor et al found Moderately, differentiated PCa (GSs 5-7) accounted for 58.1% of cases, while poorly differentiated cases (GSs 8-10) accounted for 33.8% of cases, and well-differentiated cases (GSs 2-4) accounted for the least number of cases (8.1%).[27]

5. Conclusion

PSA is most important test used in screening, diagnosis and management of prostate cancer. Its level increases approximately in proportion to the volume of prostate cancer. However, elevated serum levels of PSA do not always result from prostate cancer. Benign conditions, such as bacterial prostatitis, urinary retention, and benign prostatic hyperplasia (BPH), may also cause elevations in serum PSA levels. PSA is a valid and sensitive marker and may be continued as an early marker for the screening of prostate cancer. Serum PSA is elevated marginally in patients with BPH without inflammation and patients with chronic inflammation. Histopathological diagnosis and grading plays an important role in the management of

prostatic cancer. For satisfactory management of patient, a high degree of the awareness of the advances along with team approach has become imperative.

6. Source of Funding

None.

7. Conflict of Interest

None.

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