ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
Index Copernicus Value: 49. 23
PubMed - National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 4, Issue – 2, March - 2019, Page No. : 21 - 26

Study of Various Histopathological Lesions of Prostate and Their Correlation with Serum Prostate Specific Antigen

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Type of Publication: Original Research Paper

Conflicts of Interest: Nil

Abstract

Background: Carcinoma of the prostate is most common non skin cancer in the west and the second leading cause of cancer death among men. In India, carcinoma of prostate occupies 2nd to 10th rank among cancers in men. The present study includes description of incidence of various lesions of prostate, their clinical manifestations, serum PSA level, classification, and grading of prostate tumors.

Methods: The present study was conducted 226 prostatic needle biopsies in Department of Pathology, S. P. Medical college, Bikaner. Materials for the study consisted of prostate needle biopsies. The section were examined for histomorphological characters of prostate and clinical history was taken. The PSA levels were estimated. 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: Disease was prevalent in 7th and 8th decade of life with most common type of lesion was benign followed by malignant. Majority of 55% of benign lesions were found to be associated with serum PSA level <4ng/ml and 31.5% malignant lesion were found to be associated with serum PSA level 20.1-40.0 ng/ml. Most common gleason score was 7.

Conclusion: In conclusion benign prostatic hyperplasia is the most common pathology encountered in prostatic specimens. PSA is specific for prostatic tissue and is raised in both benign and malignant lesions of prostate.

Keywords: Gleason score, Histopathology, Prostate specific antigen, Prostate carcinoma.

Introduction

Prostate is an accessory genital gland that is part of the male reproductive system. Prostate is fibromusculoglandular organ encircling the neck of the urinary bladder. So, enlargement of prostate either due to nodular hyperplasia, prostatic intraepithelial neoplasia or adenocarcinoma may give rise to bladder outlet obstruction.[1, 2]

The incidence of prostatic lesions increases with increasing age. In the aging male, there is significant tissue remodeling taking place within the prostate. It was postulated that the growth is the result of a disturbed balance between apoptotic and proliferative activities with

net reduction in apoptotic activity. Histologic analysis showed a decreased apoptotic activity in glandular and basal epithelial cells of the prostate. Thus, with increasing age there is a tendency of increasing prostatic volume.[3-5]

Prostate-specific antigen (PSA) is a 33 kDa serine protease from the normal secretory epithelial cells of the prostate which is secreted into the prostatic ductal system. It catalyses the liquefaction of seminal coagulum. Normal levels of PSA are usually less than 4 ng/ml, but they vary according to the age of the patient.[6]

PSA is elevated by any change that disrupts the normal architecture of the prostate which allows diffusion of protease into the microvascular circulation. Raised serum PSA levels are seen in prostatitis, infarcts and benign prostatic hyperplasia, but the most clinically important elevations are seen with prostatic adenocarcinoma.

Diseases primarily inflicting prostate gland are inflammation, benign nodular enlargement, and tumors.[7] Worldwide benign prostatic hyperplasia (BPH) affects 210 million males and is common over the age of 50 years.[7,8] Carcinoma of the prostate is most common non skin cancer in the west and the second leading cause of cancer death among men.[8, 9] Carcinoma is a disease of elderly men occurring at age 65 years and above; with increasing trend in Asian countries in last 25 years. In India, carcinoma of prostate occupies 2nd to 10th rank among cancers in men, in various metro cities as per national cancer registry.[10, 11]

Prostatic carcinoma is an important growing health problem, presenting a challenge to urologists, radiologists and pathologist.[12] The incidence of prostatic diseases, benign prostatic hyperplasia, and carcinoma increases with age.[13]

Several factors, including age, race, family history, hormone levels, and environmental influences are suspected to play a role in pathogenesis.[7]

Diagnosis of prostatitis is very necessary as they can be successfully treated with antibiotics.[7] PSA is used widely as a screening tool for prostatic carcinoma. Even though considerable efforts have been taken to improve the diagnostic quality of prostatic carcinoma, screening and staging parameters are still in the primitive stage.[14]

There has been an ongoing search for a tumor marker more sensitive and specific for prostate cancer than Prostate Acid Phosphatase (PAP). Due to simplicity and cost effectiveness which are the essential characteristics of a screening test, PSA remain essential for prostate cancer diagnosis and management.[15]

Although, increased PSA levels have been found to be closely associated with prostate cancer, there can be different reasons for an elevated PSA level, including benign prostatic hyperplasia, prostatitis, prostatic trauma, and prostatic infarction.[16] Gleason grading is one of the most powerful predictors of biological behavior and influential factors used in determining treatment.[7]

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 Sardar Patel Medical College and A.G. of Hospitals and assess their incidence, prevalence and study of the various histological types and their correlation with PSA.

Material and Methods

The present study was conducted 226 prostatic needle biopsies in Department of Pathology, S. P. Medical college, Bikaner.

Materials for the study consisted of prostate needle biopsies obtained from patients clinically diagnosed as nodular hyperplasia of prostate and carcinoma of prostate. These patients were classified in different type of prostatic lesions based on histomorphological analysis of prostate biopsies.

Prostate needle biopsies for the study were obtained by needle biopsy which were performed by the Surgeons. These biopsies were kept in 10% formalin and bouin's fixative and the clinical data regarding detailed clinical history with special reference to the age of patients and duration of urinary symptoms and finding of physical and local examination and provisional clinical diagnosis.

Following adequate fixation for about 12-24 hours the tissues were submitted to routine processing, following which the paraffin embedded serial section of 4-5 microns thickness were obtained, which were stained with Hematoxylin and Eosin for morphological assessment and categorization of prostatic lesions. The section were examined for histomorphological characters of prostate and C**linical history was taken.** The PSA levels were estimated.

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.

Data Entry and Analysis

Data was entered and analyzed by using Microsoft excel version 2007 and Statistical Package for Social Science ver. 22 (SPSS.22) and necessary and appropriate statistical tests were applied and p- value <0.05 was considered statistical significant.

Results and 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. PSA is the preferred serum marker for Prostatic carcinoma[17]. Unfortunately, PSA is specific for prostate tissue but not for prostate cancer. It is also found in abnormal concentrations in normal and benign changes of the prostate such as BPH and other non-neoplastic prostatic lesions[18]. We received total 226 prostate needle biopsies in our Department of Pathology, S .P. Medical College, Bikaner.

In our study the mean±Sd of age is 69.7±9.9 years with 37.6% cases were in age group 61-70 years followed by 29.6% cases were in age group 71-80 years. In consistent with this Khant et al found 66.9 ± 9.4 years.[19] 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.[20] 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%).[21]

Here, most common type of lesion was benign (57.9%) followed by 39.4% malignant lesions and 2.7% 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.[19] Jayapradeep et al found 125 (73.5%) cases of NPH, 31 (18.2%) cases of prostatic adenocarcinoma.[20] Maru et al found 81.5% Benign and 6.87% adenocarcinoma.[18] Hirachand et al found 79.69% cases of benign and 20.31% cases of malignant type.[21]

Fig: 1 shows histopathological diagnosis in case studies. Out of total pure inflammatory lesions cases, 1 case (16.7%) had acute, 3 (50%) chronic and 2 (33.3%) granulomatous lesions. From total benign lesion, 52 (39.7%) cases had BPH with prostatitis, 78 (59.5%) had BPH without prostatitis and 1 (0.76%) cases had PIN. Out of total Malignant lesions, 88 (98.9%) cases had adenocarcinoma and 1 (1.1%) 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.[22] Sharma et al found 86.4% Chronic prostatitis followed by 9.8% Acute prostatitis and 3.7% Granulomatous prostatitis.[23]

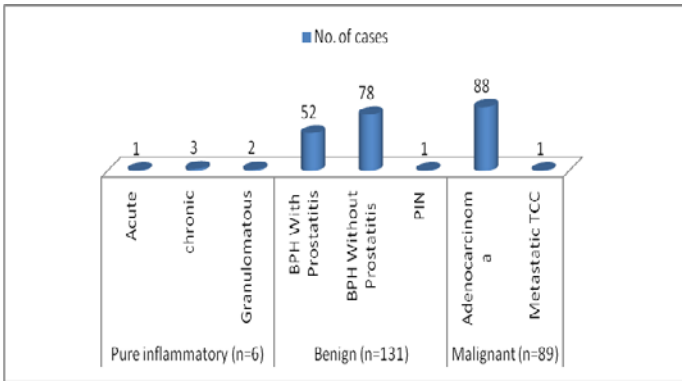

Fig: 1 Histopathological diagnosis in case studies

Table: 1 PSA Level in Various Prostatic Lesions.

PSA Level (ng/ml)	Pure Inflammatory Lesion		Benign Lesion		Malignant Lesions	
	No.	%	No.	%	No.	%
<4	3	50	72	55	4	4.5
4.1-10.0	0	0	8	6.1	0	0
10.1-20.0	3	50	31	23.7	1	1.2
20.1-40.0	0	0	15	11.4	28	31.5
40.1-60.0	0	0	4	3.04	20	22.5
60.1-80.0	0	0	1	0.76	14	15.7
80.1-100.0	0	0	0	0	7	7.7
>100.0	0	0	0	0	15	16.9
Total	6	100	131	100	89	100
Chi Square Value=37.8; d.f.=1; p=0.0001						

Here, 50% of pure inflammatory prostatic lesions were associated with serum PSA level <4ng/ml and 10.1-20.0 ng/ml. Majority of cases 72 (55%) of benign lesions were found to be associated with serum PSA level <4ng/ml followed by 23.7% cases were associated with PSA level between 10.1-20.0% ng/ml. 31.5% prostate carcinoma cases with PSA level in range of 20.1-40.0 ng/ml followed by 22.5% cases were found to be associated with PSA level 40.1-60.0 ng/ml (Table: 1). On considering serum PSA cut off value>4ng/ml, we found it's sensitivity 94.7%, specificity 59.03% and positive predictive value 54.9% and negative predictive value 95.5%. In consistent with this study by Murthy et al found that in benign lesions 13 cases had serum PSA level between 0-4 ng/ml, 22 cases had serum PSA level between 4.1-10 ng/ml, 18 cases had serum PSA level between 10.1-20 ng/ml, 11 cases had serum PSA level between 20.1-100 ng/ml and 7 cases had serum PSA level >100 ng/ml.[24] 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.[19] Koteswari and Sudhakar[25] found 25% malignant cases having PSA level 0-≤4 ng/ml, 75% malignant cases having PSA level >10 ng/ml.

Fig: 2 show Distribution of Malignant Cases According to Gleason Score. There were no cases having Gleason grade of 1, 2 and 10. 1 (1.13%) cases of each Gleason grade of 3 and 4 and 5, 18 (20.5%) cases had a Gleason score of 6, 36 (40.9%) cases had a Gleason score of 7, 26 (29.5%) cases had a Gleason score of 8 and 5 (5.7%) cases had a Gleason score of 9. 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]

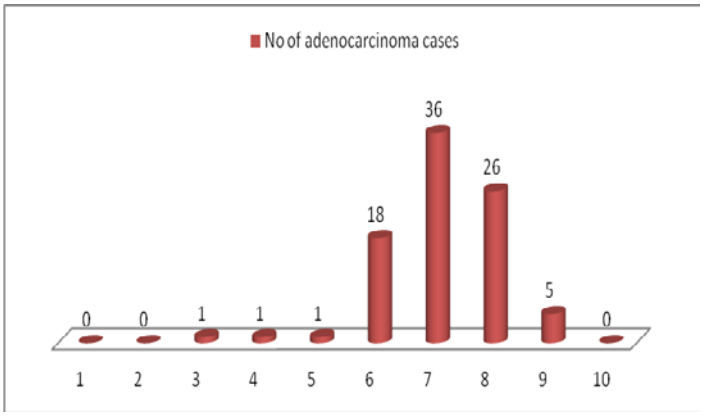

Fig: 2 Distributions of Malignant Cases According to Gleason Score.

Conclusion

In conclusion benign prostatic hyperplasia is the most common pathology encountered in prostatic specimens. PSA is specific for prostatic tissue and is raised in both benign and malignant lesions of prostate. But the chances of malignancy increases with rising value of PSA.

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