

Histological Spectrum of Prostatic Adenocarcinomas in Correlation with PSA Values

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Abstract

Background & objectives: Histopathology is the gold standard in the diagnosis and management of prostatic adeno carcinomas. The objectives of this study are

- 1) To determine the age distribution and clinical presentation of patients with prostatic adenocarcinomas
- 2) To study various Gleason's microscopic patterns of prostatic adenocarcinomas
- 3) To assign them with Gleason's score
- 4) To correlate Gleason's score with prostatic specific antigen values in these cases.

Methods: The study was done on 370 prostatic specimens over a period of 4 years from June 2011 to June 2015 which included both transurethral resection of prostate chips and needle core biopsies received in the department of Pathology, NRI Medical College, Chinakakani. The study included only prostatic adenocarcinomas which constituted to 75 cases out of 370 cases, with the incidence of 20.3%

Results: Prostatic adeno carcinomas were common in the age group of 70-79 years with the three common symptoms of dysuria, incomplete voiding and frequency. The most common primary microscopic pattern was Gleason's pattern 3, followed by pattern 4. The most common Gleason's score was 7 (43%) which showed PSA values in the range of 21-50 ng/ml. The p value for serum PSA levels and Gleason score was 0.00001.

Interpretation & Conclusions: The present study showed a strong correlation between Gleason's score and PSA values. It is concluded that as the Gleason's score increases the serum PSA values also increases

Key words: Adenocarcinoma of prostate; Gleason's score; Prostate specific antigen; Trans urethral resection of prostate.

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Introduction

The prostate is a retroperitoneal organ encircling the neck of bladder and urethra. It is the largest accessory reproductive organ in male and is an exocrine gland whose secretions form significant component of seminal fluid. Prostatic carcinoma is now the sixth most common malignancy in the world (in terms of number of new cases) and third in importance in men. It represents 9.7% of cancers in men (15.3% in developed countries and 4.3% in developing countries).⁽¹⁾ It is predominantly a disease of elderly. Prostate cancer is responsible for 3% of all deaths in men over age of 55 years.⁽²⁾ Unlike other Asian countries, India has a fairly high incidence of prostatic carcinoma.⁽³⁾ As the diet in Asia becomes more westernized, the incidence of clinically significant prostate cancer in this region seems to be increasing.⁽⁴⁾

Etiology of prostatic carcinoma is largely unknown till today, rendering disease prevention

difficult. Hereditary factors have a role.^(5,6) The great differences in the incidence of clinically manifest carcinoma indicate that the nutritional and environmental factors also may have an influence on the development and progression of the disease.⁽⁷⁾ Diet rich in animal fat especially red meat show strong positive association for development of prostatic carcinoma.⁽⁸⁾ Low levels of dietary selenium, vitamin E and vitamin D also play a role.⁽⁹⁾ Studies also reveal that there is no definite role of sexual activity, smoking, height & weight of the individual and alcohol consumption.⁽¹⁰⁾

Prostatic carcinoma has to be given importance as its incidence is increasing. This study comprises description of various Gleason's microscopic patterns of prostatic adeno carcinomas encountered in our institution, their associated clinical manifestations and also serum Prostatic Specific Antigen (PSA) level correlations in these cases. It is more necessary to study prostatic carcinomas in the present situation as their incidence keeps growing due to extended male longevity past the 60's.

Materials and Methods

The present study was undertaken on all the prostatic specimens received in the histopathology department of our institute, during the period of 4 years, from June 2011 to June 2015. The prostatic material

included prostatic biopsies and transurethral resection of prostatic [TURP] chips. Our study included 370 prostatic specimens. Of which a total of 75 prostatic adenocarcinoma cases only were included in the present study. The material included 60 cases of prostatic needle biopsies and 15 cases of transurethral resection of prostatic chips. The clinical details were obtained from the case files and electronic medical records across hospital information systems.

In cases of prostatic biopsy, entire tissue received was fixed and processed. In cases of TURP chips, 3 to 4 cassettes were prepared in each case accommodating the total tissue and weighed approximately 8-10 grams. Specimens weighing less than or equal to 12 grams were submitted entirely. In cases of excess material one additional cassette for each additional 10 grams of tissue was prepared.

Generally, random chips were submitted for processing; however, if some chips were firmer or had a yellow or orange-yellow appearance, they were preferentially submitted. If carcinoma was detected in a TURP specimen, then all the remaining tissue was processed entirely to ensure thorough examination with reference to the pattern and scoring of malignancy.

All the tissues were fixed in 10% buffered formalin and paraffin embedded. 3 to 5 micron sections were cut and stained with routine Hematoxylin and Eosin (H & E) stain. All the slides were thoroughly evaluated and the prostatic adenocarcinomas were graded by using Gleason microscopic grading.

Inclusion criteria: Only prostatic adenocarcinomas.

Exclusion criteria: Any prostatic tissue other than prostatic adenocarcinoma.

Results

The present study was carried out only on prostatic adenocarcinoma cases constituting to 75 cases out of 370 prostatic specimens received in our institution over a period of 4 years from June 2011 to June 2015. The incidence of prostatic adenocarcinoma in the present study was 20.3%. The age group of these cases ranged from 50 - 93 years with the mean age of 70 years. 30 cases (40%) out of 75 cases of prostatic adenocarcinoma were in the age group of seventy to seventy nine years (Table-1). The patients of prostatic adenocarcinoma have presented with three common symptoms of dysuria, incomplete voiding and frequency each constituting to 26.67% (Table-2). Gleason grading system based on glandular architecture defines five histological patterns or grades with decreasing glandular differentiation. Gleason's pattern 3 was the most common pattern in the present study. The second most common Gleason's pattern was pattern 4 (Table-3). Gleason's score was obtained by adding the primary (most predominant) Gleason grade and the secondary (second most predominant) Gleason grade. When no secondary Gleason grade exists, the primary Gleason grade was

doubled to arrive at a Gleason score. Among all the 75 prostatic adenocarcinoma cases studied the most common Gleason's score was 7 in 32 cases constituting 43%, followed by score 5 (17%), score 8 and 9 (12% each) (Table-4). The adjacent tissue in most of the prostatic adenocarcinoma cases showed nodular hyperplasia as accompaniment. Out of 75 prostatic adenocarcinoma cases, there was coexistence of other lesions such as nodular hyperplasia in 55 cases, chronic prostatitis in 15 cases and High grade prostatic intraepithelial neoplasia [HGPIN] in 05 cases (Table-5). PSA levels which play an important role in the early detection and screening of prostatic cancer were obtained in all the malignant cases studied. Its value ranged from 4.1 – 70 ng/ml. The serum PSA values were correlated with Gleason's score and showed a positive correlation with statistically significant p value (Table-6)

Discussion

In cancer related deaths in men, the prostatic cancer is the second only to lung cancer⁽¹¹⁾. Prostate cancer is responsible for 3% of all deaths in men over age of 55 years.⁽²⁾ The results of the data analysis in the present study which comprises 75 cases of prostatic adenocarcinoma showed that adenocarcinoma of prostate was common in the age group of 70-79 years (Table-1) with the mean age of presentation being 70years. The youngest patient was 50 years and the oldest was 93 years.

According to study done by Brawn et al⁽¹²⁾, the average age of presentation for adenocarcinoma of prostate was 67 years. In a study done by Quian et al.⁽¹³⁾ the mean age for carcinoma was 64.4 years (44 to 77years). Our findings were similar to these studies.

The various clinical presentations of prostatic diseases can be grouped as obstructive or irritative lower urinary tract symptoms. Irritative symptoms included urgency, increased frequency, dysuria and nocturia. Obstructive symptoms included hesitancy, weak stream, terminal dribbling and acute or chronic retention of urine. In the present study the malignant lesions had 3 common symptoms of dysuria, incomplete voiding and frequency of micturition (Table-2). The incidence of prostatic adenocarcinoma was 20.3% in this study. There is wide variation in the incidence rate of prostate cancer in different parts of the world. According to the study done by Chandanwale Shirish et al⁽¹⁴⁾ on 100 prostatic specimens over a period of 2 years from 2010 to 2012, the incidence of prostatic carcinoma was 17%. According to the study done by Richard Babaian et al⁽¹⁵⁾ on 151 prostatic specimens between September 1998 and September 1999 at university of Texas M.D Anderson cancer center, prostatic cancer was detected in 24.5% of men biopsied. Bob Djavan et al⁽¹⁶⁾ reported 22% incidence of carcinoma. Our findings are similar to these studies

According to the study done by Bob Djavan et al⁽¹⁶⁾, the mean age of patients was 67yrs and mean Gleason's score was 6. Richard Babaian et al⁽¹⁵⁾ reported the mean age as 62yrs (range 43-74) and the Gleason score was 6 in 12 patients 7 in 1 and 8 in 1 in his study. The findings of the present study were similar to these studies with the mean age of 70 years and mean Gleason's score of 7.

Gleason's grading system was used in the present study which is most popular worldwide. Important features of various patterns can be summarized as follows:

Pattern-1: Closely packed, single, separate, round, uniform glands with well-defined margins.

Pattern-2: Similar to pattern 1, but the glands are less uniform and less well defined margins (Figure- 1).

Pattern-3: The size of glands is variable. Both small and large glands and a papillary or cribriform pattern appear. Margins are poorly defined (Figure- 2).

Pattern-4: Small fused glands; the glands may have papillary, Cribriform or solid pattern (Figures-3, 4).

Pattern-5: Few discernible glands; a comedo pattern is usually present. Tumor cells infiltrate the stroma as single cells or as ill-defined cords. The presence of necrosis in any pattern automatically upgrades it to pattern 5 (Figures- 5, 6).

PROSTATIC ADENOCARCINOMA Gleason Microscopic Patterns

Gleason Pattern 2

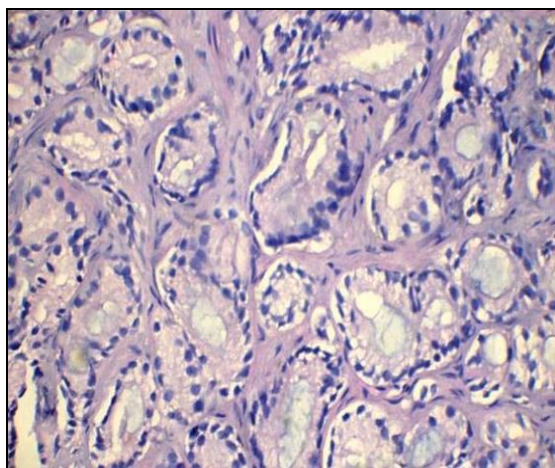


Fig.1: Photomicrograph of Gleason pattern 2. Uniform looking round to oval glands with smooth ends. (H&E X 100)

Gleason pattern 3

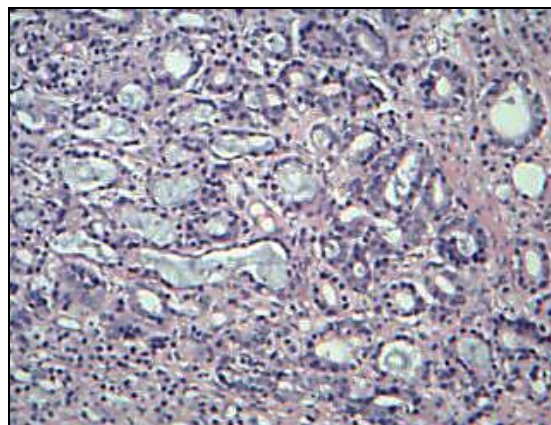


Fig. 2: Photomicrograph of Gleason pattern 3. Small, variably sized and shaped glands often angular (H&E X 100)

Gleason pattern 4

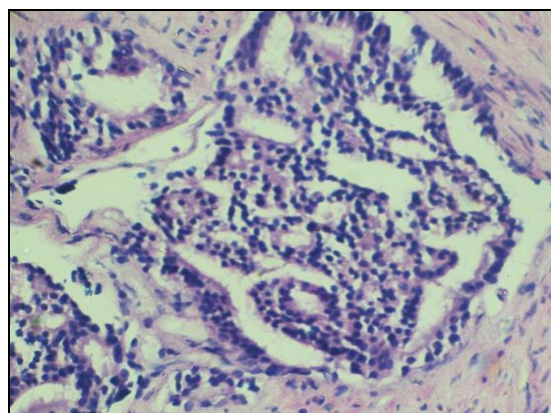


Fig. 3: Photomicrograph of Gleason pattern 4 with large cribriform glands (H&E X 100)

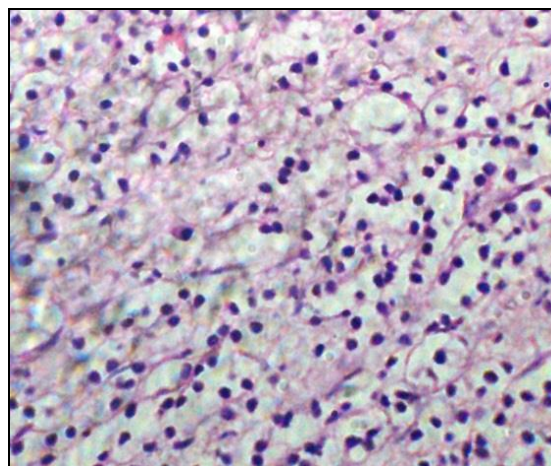


Fig. 4: Photomicrograph of Gleason pattern 4 showing hypernephroid pattern of fused glands(H&E X 400)

Gleason pattern 5

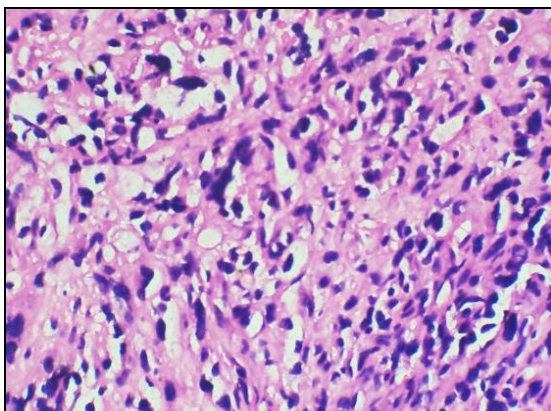


Fig. 5: Photomicrograph of Gleason pattern 5 showing, solid sheets with loss of glandular lumina (H&E X 100)

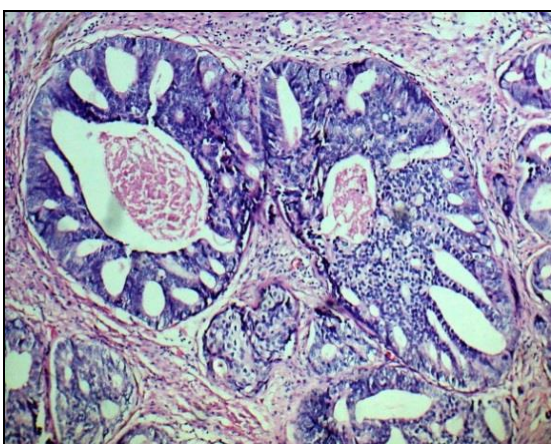


Fig. 6: Photomicrograph of Gleason pattern 5 with comedo necrosis (H&E X 100)

GLEASON SCORE 7 (3+4)

(The most common Gleason score in this study)

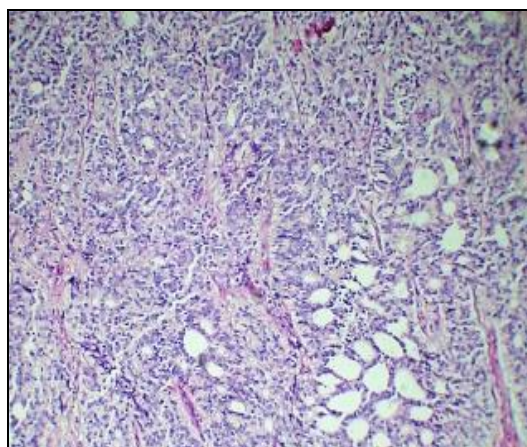


Fig. 7: Photomicrograph showing Gleason Score of 7(3+4), primary pattern being 3 & Secondary pattern being 4 (H&E X100)

PERINEURAL INVASION

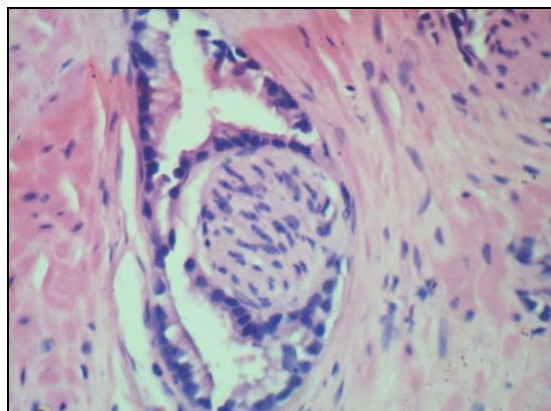


Fig. 8: Photomicrograph showing perineural invasion (H&E X400)

The Gleason's score is obtained by adding the primary (most predominant) Gleason grade and the secondary (second most predominant) Gleason grade. When no secondary Gleason grade exists, the primary Gleason grade is doubled to arrive at a Gleason's score.

Tertiary pattern is least common pattern and should be reported in diagnosis only if it is Gleason's pattern 4 or 5. It should be reported even if it is less than 5%, because presence of even small amount of high grade tumor affects the prognosis.

Gleason grade 3 was the most common primary pattern in our study (Table-3). The most common secondary pattern was Gleason grade 4, while tertiary pattern was not identified. And the most common Gleason's score was 7 (Figure-7) in 43% cases, 5 in 17% of cases, 8 and 9 in 12 % of cases, 6 and 4 in 8 % of cases (Table-4). 05 cases of prostatic adenocarcinoma showed the evidence of perineural invasion with circumferential involvement of the perineural space (Figure-8). In a study done by Babaian RJ et al⁽¹⁵⁾. The overall Gleason scores in 244 cases were 4(one case 0.4%), 5(63 cases 25.81%), 6(114 cases 46.72%), 7(151 cases 61.88%), 8(9 cases 3.68%), and 9 (26 cases 10.65%). The overall Gleason score in the study done by Falzarano et al⁽¹⁵⁾ was 6 in 21 (34%), 7 in 34 (55%) and 9 in 4 (6%) cases. Our findings are almost similar with the studies of Babaian et al⁽¹⁵⁾ and Falzarano et al.⁽¹⁷⁾

In our study, out of 75 cases of prostatic adenocarcinoma, 05cases were found in association with HGPIN constituting to 6.6% of total prostatic adenocarcinomas (Table-5). The findings are similar to the studies done by Pacelli et al⁽¹⁸⁾ and Chandanwale Shirish et al.⁽¹⁴⁾ Prostate specific antigen (PSA) is considered as the best marker for prostatic carcinoma. Normal serum PSA is 0-4ng/ml. In the present study, serum PSA levels were available in all the 75 malignant cases and they showed an increase in serum PSA with an average PSA value of 29.3ng/ml. The present study

showed strong positive correlation between Gleason score given in prostatic adenocarcinomas and serum PSA values with a p value of 0.00001 (Table 6). The results were similar to the studies done by Karazanashvili G et al⁽¹⁹⁾ and Wei -Jen Shih et al⁽²⁰⁾, with the p values of 0.047 and 0.05 respectively.

Thus to conclude, in the present study the incidence of prostatic adenocarcinoma was 20.6%, the common age group was in the range of 70-79 years with common clinical presentations being dysuria, incomplete voiding and frequency of micturition. Gleason grade 3 was the most common pattern seen and the majority of the cases were of Gleason's score 7 with a strong correlation between serum PSA levels and Gleason's score indicating that as the Gleason's score increases the serum PSA values also increases.

Table 1: Age incidence among prostatic adenocarcinomas in the present study

Age group	No. of cases
40-49	-
50-59	07
60-69	26
70-79	30
80-89	11
90-99	01
Total no. of cases	75

Table-2: Clinical presentation

Clinical symptoms	Number of cases (%)
Frequency	20 (26.67%)
Nocturia	01 (1.33%)
Urgency	-
Difficulty in voiding	10 (13.34%)
Straining	-
Poor stream	-
Hesitancy	-
Incomplete voiding	20 (26.67%)
Hematuria	02 (2.66%)
Acute retention	02 (2.66%)
Dysuria	20 (26.67%)
Total no. of cases	75 (100%)

Table 3: Gleason's microscopic patterns in malignant lesions studied

Microscopic findings	Pattern	Number of Cases
Loosely arranged round glands	2	25
Small, variably sized glands	3	61
Fused glandular with cribriform pattern	4	48
Hypernephroid pattern	4	03
Solid sheets	5	12
Comedo necrosis	5	01

Table 4: Incidence of prostatic adenocarcinoma with reference to Gleason's score

Gleason score	No. of cases
2	-
3	-
4	06 (8%)
5	13 (17%)
6	06 (8%)
7	32 (43%)
8	09 (12%)
9	09 (12%)
10	-
Total	75 (100%)

Table 5: Microscopic findings in adjacent prostatic tissue in adenocarcinoma cases studied

Microscopic findings	No. of cases
Adenofibromyomatous hyperplasia	55
Chronic prostatitis	15
HGPIN	05
Total	75

Table 6: PSA values among adenocarcinomas with various Gleason's score

Gleason's score	4-10 ng/ml	11-20 ng/ml	21-50 ng/ml	>50 ng/ml
3	-	-	-	-
4	6	-	-	-
5	6	7	-	-
6	-	6	-	-
7			32	-
8			8	1
9				9

p value of 0.00001

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