

The Histopathological Patterns of Prostatic Diseases and Prostatic Cancer in Yemeni Patients

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Abstract

Objective: The aim of this retrospective study was to delineate the histopathologic patterns of prostatic diseases and prostatic cancer in Sana'a Yemen. **Methods:** This is a descriptive record-based study of 1188 cases of prostatic diseases was carried out in the department of pathology, Faculty of Medicine and Health Sciences, Sana'a University, Sana'a Yemen during the period from 1st January 2004 to the 30th December 2012. The diagnosis was made on hematoxylin and eosin stained sections and categorized the cases of prostatic diseases and prostatic cancer according to histological diagnosis. **Results:** Out of 1188 cases of prostatic diseases, 713 (60%) were benign prostatic hyperplasia (BPH), followed by BPH with inflammation 276 (23%). The prostatic neoplasms accounted, for 199 (16.8%). The commonest type of neoplasms was adenocarcinoma comprising 174 cases (14.6%). The rest of cases were eighteen focal atypical intraepithelial neoplasm, two nodular leiomyoma, two urothelial carcinoma, one undifferentiated spindle cell malignancy and last one was high grade stromal phylloides like sarcoma. The mean and median age, for adenocarcinoma was 69 and 70 years respectively. In BPH the mean age was 66 years, and the median age is 70 years. Gleason's score 6 was the most frequent 51 (36.4%) in occurrence followed by score four 34 (24.3%). Adenocarcinoma and BPH were accountable for prostatic specific antigen (PSA) levels of 1 to 50 ng/ml, while values of 51ng/ml and above were seen exclusively in adenocarcinoma. **Conclusion:** BPH was the common prostatic lesion with peak incidence in six and seven decades. Adenocarcinoma of Gleason's score 5 to 6 (moderately differentiated) was the most frequent grade. Screening protocols and awareness programs of prostatic cancer need to be introduced in this country.

Key words: Benign prostatic hyperplasia - Adenocarcinoma- Prostatitis- Prostatic specific antigen - Gleason's score- Yemen.

INTRODUCTION:

Prostatic diseases are responsible for significant morbidity and mortality among adult males worldwide¹. Most frequently encountered diseases affecting prostate are prostatitis, benign prostatic hyperplasia (BPH) and prostatic cancer¹. Prostate cancer is the most common malignant tumor in men all over the world and is also the second important cause of cancer related deaths in men after lung cancer². The average age at the time of diagnosis is about 67 year. Prostate cancer can be a serious disease, but most men diagnosed with prostate cancer do not die from it³. Adenocarcinoma is the most common histological variant of prostatic cancer¹. Once the diagnosis of cancer is made, tumor grading, especially the

Gleason score, strongly influences decisions regarding options for therapy⁴. However, the most important risk factors for developing prostate carcinoma are family history, increasing age, lack of exercise and high calcium intake⁵. BPH or nodular hyperplasia is the non-malignant adenomatous growth characterized by hyperplasia of stroma and epithelial parenchyma, resulting in the difficulty of urination and in extreme cases, completely impossible^{6,7}. Statistical observations suggest that a diet low in fat and red meat and high in protein and vegetables, could protect against BPH⁸. Inflammation of prostatic gland is characterized by urinary frequency, dysuria, body aches and sometimes fever. It is estimated that number of males in the United States who will experience prostatitis

during their lifetimes range up to 50%⁹. The recent global perception of a rising incidence of prostatic diseases necessitates detailed descriptions of the patterns in view of the known geographical variations. In Yemen no study has, been undertaken to document the histopathological patterns of prostatic lesions, hence the need for this study.

Methods: A descriptive record-based study of 1188 cases of prostatic lesions was carried out in the department of pathology, Faculty of Medicine and Health Sciences, Sana'a University, Sana'a Yemen, spanning a period of nine years from 1st January 2004 to the 30th December 2012. The diagnosis was made primarily in Aulagi private laboratory in Sana'a who received the histopathologic biopsies from Sana'a and other Yemeni provinces. Most of the Yemeni patients are referred to Sana'a for further investigations and therapy, where most of the surgeons, oncologists and pathologists, are practicing. The biopsies, trans-urethral resection and total resection sections were fixed in 10% formalin solution before being processed by manual and automatic tissue processor. These sections were stained with hematoxylin and eosin stain for routine histological diagnosis. During the histological study the sample was evaluated regarding the pathological changes, nodularity, inflammatory reaction, morphology of parenchyma and stroma, malignant features and arrangement of cancer cells as well as grading of cancer according to Gleason scoring. Finally, the cases were categorized into the main histological patterns; BPH, BPH with inflammation, BPH with focal intraepithelial neoplasm, adenocarcinoma, and other rare types. The clinical data were collected from the request forms. The present study focuses on those cases that revealed pathological change and excludes the cases showed negative pathological changes and cases revealing doubtful change of malignancy.

Results: Out of 1188 cases of prostatic diseases, 713 (60%) were BPH, followed by BPH with inflammation 276 (23%); 233(19.6%), chronic inflammation, 41(3.5%) chronic prostatic urotheritis and two cases acute

prostatitis. The prostatic neoplasms accounted for 199 (16.8%). The commonest type of neoplasms was adenocarcinoma comprising 174 cases (14.6%). The rest of cases were eighteen focal atypical intraepithelial neoplasm, two nodular leiomyoma, two urothelial carcinoma, one undifferentiated spindle cell malignancy and last one was high grade stromal phylloides like sarcoma. Table 1. The mean and median age, for adenocarcinoma was 69 and 70 years respectively. In BPH the mean age was 66 years, while and the median age is 70 years Table 2. Gleason's score six was the most frequent 51 (36.4%) in occurrence followed by score four 34 (24.3%) Table 3. Adenocarcinoma and BPH were accountable for prostatic specific antigen (PSA) levels of 1 to 50 ng/ml, while values of 51ng/ml and above were seen exclusively in adenocarcinoma Table 4.

Discussion. There are three important lesions of prostate, these include prostatitis, BPH, and cancer, and they are responsible for significant morbidity and mortality among adult males¹. In our study, mean age of patients was 67.5 years and most of the cases of BPH and cancers were present in six and seven decades. These findings were similar with reports documented in Pakistan, Oman, and Saudi Arabia ^{10,11,12}. BPH was the most common frequent lesions in our report 83.2% which was frequently found in the age groups of six and seven decades. A study in Pakistan¹⁰ and India¹³ showed somewhat higher frequency of BPH 87% and also same age group. A reports from Saudi Arabia¹² showed slightly lower frequency 82%, while a study from Nigerian¹ showed 72.2% of frequency but the peak age of incidence was similar to our findings. The variation that exist between different places and countries may be simply due to variation in diagnostic criteria, number of patients studied, and due to differences of prevalence or susceptibility to risk factors. In our study we found that frequency of BPH increases with age from fifth decade to eight decade, this reflects that hyperplasia process is impaired cell death due to which there is an overall reduction in the rate of cell

death, resulting in the accumulation of senescent cells in the prostate. It is believed that dihydrotestosterone – induced growth factors cause increase proliferation of stromal cells and decreasing the death of epithelial cells. Microscopically hallmark of BPH is nodularity. Early nodules are composed of stromal cells and later predominantly epithelial nodules arise. From their origin, nodular enlargement encroaches into lateral walls of urethra¹⁴. In current study many of the cases of BPH were associated with inflammation 23.2%. In one article from Saudi Arabia chronic prostatitis was observed in 95.1% of all biopsied reviewed¹². After BPH, prostatic adenocarcinoma was found to be the commonest lesion 14.6%, occurs mostly in the same age group as BPH i.e. 60-70 years. Same findings were also reported in a study conducted in Faisalabad, Pakistan 13.2%⁷. However, as compared to our study, in Oman, India, and Saudi Arabia there was a slight lower incidence 10% was seen^{11,12,13}. Further, in contrary to our study, study in India showed peak age of incidence in the eight decade of life¹³. The data from USA in 2006 and Europe in 2008 reveals that prostatic cancer is the commonest disorder in men^{15,16}. Androgen plays an important role in pathogenesis of prostate cancer. They bind to the androgen receptors and induce the expression of pro-survival and pro-growth. Over expression makes normal prostate epithelial cells more invasive¹⁴. When PSA was elevated to 4-10 ng /ml, cancer was detected in 21.4%. Elevation of PSA to 10-20 ng /ml lead to cancer detection in 40% of the patients and when PSA was more than 20 ng /ml all cases were considered positive for cancer¹⁷. In our study, among the cancer patients, PSA values ranged between 5.4 ng /ml to 529 ng /ml, these findings shown in Table 4, denote that using the PSA cutoff value of 4 ng /ml for prostatic biopsy is sufficient and no need to decrease the cutoff value of PSA to 2.5 ng /ml. Recently, some authors have recommended lowering the total serum PSA cutoff for prostatic biopsy from 4 ng /ml to 2.5 ng /ml^{17,18}. Prostatic carcinoma were graded according to the

Gleason's scoring. Notably, in our current study, the Gleason's score between 5 and 6 (moderately differentiated) was account to 38.5% followed by Gleason's score between 2 and 4 (well differentiated) 35.2%. Gleason's score between 7 and 10 had poorly differentiated and accounted for, 26.3%. In a pathological study in Oman, cancers were seen in 10.9%. Most of the patients had high Gleason's score, with 65.6% having scores between 7 and 10 (poorly differentiated) and 24.8% with score 5-6 (moderately differentiated). Only 0.08% had well differentiated carcinoma with Gleason score between 2 and 4¹¹. In analysis of 83 patients of prostatic carcinoma from Saudi Arabia shows vast majority of carcinoma 92.8% have Gleason sum of 6 or more, while only 3.6 had Gleason score 4¹⁸. Hence, worth to mention, the incidence of prostatic carcinoma is low in Yemen, it is usually take places as mostly moderately differentiated disease. The data for this study have principally been obtained from private laboratories. Therefore, it is not possible to derive specific explanations for staging, treatment and follow up. In spite of these limitation, it could serve as a baseline description of prostatic diseases in the Republic of Yemen and reveals some striking information which indicates the need for establishing a national cancer registry.

Conclusion: Benign prostatic hyperplasia was the most common prostatic lesion occurring commonly in six and seven decades. Adenocarcinoma of Gleason's score 5 to 6 (moderately differentiated) was the most frequent grade. Screening protocols and awareness programs of prostatic cancer need to be introduced and screening programs should be focused on level of PSA and digital rectal examination. Further future studies addressing this issue are needed to confirm the potential rising trend, and to evaluate the possible role of changing dietary habits and environmental risk factors.

Table 1 Overall distribution of different prostatic lesions in prostatic specimens (n= 1188)

Diagnosis	N	%
Benign prostatic hyperplasia	701	59
BPH with focal infarction	12	1
BPH with inflammation	276	23.2
Chronic prostatitis	233	
Non-specific	227	--
Granulomatous♣	6	--
Chronic prostatic urotheritis	41	--
Acute prostatitis	2	--
Neoplasms		
Adenocarcinoma	174	14.6
Urothelial carcinoma	2	0.16
Spindle cell undifferentiated	1	0.08
Embryonal rhabdomyosarcoma	1	0.08
Stromal high grade phylloides like-sarcoma	1	0.08
Benign leiomyoma nodule	2	0.08
Focal intraepithelial neoplasms	18	1.5
Low grade	9	--
High grade	9	--
Total	1188	100

♣ Four cases Schistosomiasis, one tuberculosis, one non-tuberculous granuloma

Table 2 Age distribution of adenocarcinoma and benign prostatic hyperplasia

Type Age years	Adenocarcinoma	BPH
Mean	69	66
Median	70	70
Maximum	100	104
Minimum	50	34

Table 3 Distribution of the adenocarcinoma cases according to Gleason's score⁴ (n=140)

Gleason score	2	3	4	5	6	7	8	9	10	Sum
No of cases	7	8	34	3	51	17	15	2	3	140
%	5	5.7	24.3	2.1	36.4	12.1	10.7	1.4	2.1	100

Table 4 Demonstrate the prostatic specific antigen in adenocarcinoma and benign prostatic hyperplasia

Prostatic specific antigen	Adenocarcinoma (n=37)		Benign prostatic hyperplasia (n=47)	
	No	%	No	%
< 20ng	5	13.5	39	82.9
20-50ng	7	18.9	8	17.
51-99ng	8	21.6	-	-
≥100ng	17	45.9	-	-
Total	37	100	47	100

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