RESEARCH ARTICLE

Histopathologic Characterization of Prostate Diseases in Madinah, Saudi Arabia

Abdulkader Albasri[1]*, Abeer El-Siddig[1], Akbar Hussainy[1], Mervat Mahrous[2], Abdulaziz Abdullah Alhosaini[1], Ahmed Alhujaily[3]

Abstract

Aims: To delineate the histopathological pattern of prostate diseases and to highlight age variations in prostate specific antigen (PSA) values and histopathological features. Materials and Methods: A retrospective review was made of all prostate biopsy reports seen between January 2006 and December 2013 at the King Fahad Hospital, Madinah, Saudi Arabia. Prostate lesions were tabulated and classified into benign and malignant groups. Histological scoring of adenocarcinomas was accomplished using the Gleason system. PSA values were correlated with Gleason scores. Results: Of 417 prostate lesions reviewed, 343 (82.3%) were benign and 74 (17.7%) were malignant, giving a benign to malignant ratio of 4.6:1. Benign prostatic hyperplasia (both with and without inflammation) was the commonest prostatic lesion and accounted for 80.3% of all cases and 97.6% of all benign cases. The age range was 20 to 97 years with a mean of 69.2 years and a peak age group at 70-79 years. Seventy one cases of adenocarcinoma accounted for 95.9% of the total of 74 malignant tumors. It showed an age range of 44 to 95 years, a mean age of 70.9 years and peak prevalence in the 80-89 year age group. Gleason score seven was the most frequent (39.4%) in occurrence. Most adenocarcinomas, 41 cases (57.7%), were moderately differentiated (Gleason score of 5-7). PSA values ranged widely between 16-1,865ng/ml with a mean of 363.4ng/ml. Elevated PSA (>100ng/ml) levels were found in 53 (81.6%) patients. There was a statistically significant positive correlation between serum PSA level and Gleason score (p=0.0304). Conclusions: Prostatic lesions constitute a significant source of morbidity among adult males in Madinah. Benign prostatic hyperplasia was the commonest benign prostatic lesion and adenocarcinoma was the commonest histological subtype of prostatic cancer.

Keywords: Prostate diseases - BPH - carcinoma prostate - Madinah - Saudi Arabia

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Introduction

Majority of the prostatic diseases can be grouped into either Benign prostatic hyperplasia (BPH) or Carcinoma Prostate (CaP), along with a minor miscellaneous group of inflammation, infarction etc. Globally, benign prostatic hyperplasia affects about 210 million males (Vos et al., 2012). Although BPH is predominantly attributed to aging, genetic factors and hormonal disturbances (Nicholson and Ricke, 2011), a possible role of obesity, diet and life style is also under investigation (Tewari et al., 2012; Goluch-Koniuszy et al., 2013). Similarly the significance of chronic inflammation in pathogenesis of BPH has recently emerged (Fibbi et al., 2010) and emphasized by recent publications (Vral et al., 2012; Bostanci et al., 2013; Gandaglia et al., 2013). Pathological data from Kingdom of Saudi Arabia (KSA), regarding BPH is a bit historic, however is consistent with Western findings i.e. age at presentation and major complaints (Mosli et al., 2000).

In the USA, prostate cancer is the most commonly diagnosed non–skin cancer and the second leading cause of cancer death (Brawley, 2012a). Screening programs have increased risk of diagnosis among younger men in their 40s and 50s (Brawley, 2012b). According to the Cancer Statistics Registrations, England (2011), during the year 2011, the three most common cancers for men were prostate (25.6%), lung (13.8%) and colorectal (13.6%) in England. Almost similar overview regarding CaP is available in the recent literature from all over the world i.e. from China (Na et al., 2012; Xie et al., 2012), Indonesia (Wahidin et al., 2012), Nepal (Belbase et al., 2013), India (Takiar and Kumar, 2014) and Pakistan (Ahmad et al., 2009; Jamal et al., 2014).

Within the Middle Eastern region, Iranian workers have also reported higher incidence and increasing trend of CaP in their country (Talaiezadeh et al., 2013; Basiri et al., 2014). In the Jordan cancer registry study, CaP was one of the major cancer site (Ismail et al., 2013). In a Cancer epidemiology review for the region of South-West Asia; Jews in Israel were found to have prostatic cancer as number one cancer in their population (Salim et al., 2010). In a similar comprehensive review of Cancer

*[1]Department of Pathology, Taibah University, [2]Department of Oncology, [3]Department of Pathology, King Fahad Hospital, Madinah, Saudi Arabia *For correspondence: rmor_family@hotmail.co.uk*

epidemiology in Arab world, carcinoma of the breast, prostate and colorectum appeared to be increasing in the region. In KSA, Prostate cancer was number 4 in incidence after the malignancies of liver, lung/trachea and leukemia (Salim et al., 2009).

In the KSA, one screening study from Eastern region (Dammam), CaP was confirmed in only 1.17% subjects. Therefore it was concluded that the incidence of CaP was low in that study (Taha and Kamal, 2005). On the contrary, opposite conclusion was derived from a recent similar study from Central KSA (Riyadh); it was concluded that the rate of prostate cancer detection by screening was higher than expected and the disease was advanced (Rabah and Arafa, 2010).

Regarding Hospital-based histopathological studies, extensive search in the recent literature reveal only three scholarly works from KSA; two done a bit earlier in the new millennium by Mansoor (2002) and Tayib et al. (2003), while one study was done relatively recently by Mosli et al. (2009). All these researches have been done from the Western region city of Jeddah; however there is no such work published from the region of Madinah, neither at epidemiological level nor at histopathological level. Our research work is first of its kind in the city of Madinah, in which we have analyzed the histopathological data and also focused on correlation of PSA levels with tumor grading (Gleason scores).

Materials and Methods

This retrospective study included histopathological reports of all patients who underwent histopathological examination of their prostatic biopsies either for their whole prostates, TURP or core biopsies between January 2006 and December 2013 at King Fahad Hospital, Madinah, Saudi Arabia. Histopathology slides of cases within the study period were reviewed by the authors (A.A and A.A) to make a consensus diagnosis. Data including patients' age, PSA value and histological diagnosis were recorded in a tabulated form. The prostate cancer was graded and scored according to Gleason system. The cases were classified into two main groups; benign and malignant. Comparisons of the Gleason score of prostate cancer biopsies and PSA levels was performed using unpaired students' t tests for independent samples, with a level of $p<0.05$ considered as statistically significant. Statistics were computed using SPSS version 20 (SPSS Inc. Chicago, IL).

Results

A total of 417 prostate specimens were received at the Department of Pathology, King Fahad Hospital, Madinah, Saudi Arabia from January 2006 to December 2013. The reviewed cases were classically categorized into two main groups; benign (343; 82.3%) and malignant (74; 17.7%). The age distribution of the benign prostate cases extends from 20 years to 97 years with mean age at diagnosis of 69.1 years, while in the cancer patients the earliest age at diagnosis was 44 years and the oldest was 95 years with mean age of 71.2 at time of diagnosis. Table 1 demonstrates the overall distribution of different prostatic diseases diagnosed according to pathological features.

In the benign group, benign prostatic hyperplasia (both with and without inflammation) was the commonest prostatic lesion and accounted for 80.3% of all cases and 97.6% of all benign cases. The age range was 20 to 97 years with a mean of 69.2 years and a peak age group at 70-79 years (Table 2). One hundred and fifty-six patients had benign prostatic hyperplasia with inflammation, with an age range between 35 and 97 years (mean 69.7 years). Most of the patients (n=57; 36.5%) were between 70-79 years of age. Other less common benign lesions encountered were inflammation (acute/chronic) seen in 8 patients, with an age range between 43 and 75 years (mean 69 years) (Table 2).

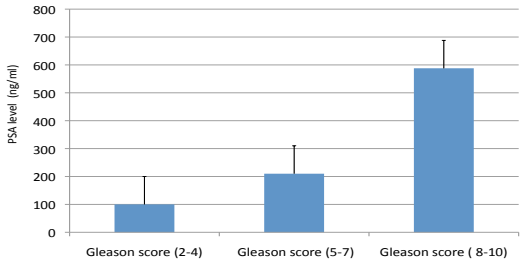

Figure 1. Correlation of PSA Levels with Gleason Score

Table 1. Overall Distribution of Different Prostatic Diseases in Prostatic Specimens (n=417)

Prostatic lesion	N (%)	Mean age years
Benign	343 (82.3)	69.1
Benign prostatic hyperplasia	179 (42.9)	68.8
Benign prostatic hyperplasia with inflammation	156 (37.4)	69.7
Inflammation	8 (1.9)	69.0
Malignant	74 (17.7)	71.2
Adenocarcinoma	71 (17.0)	70.9
Squamous cell carcinoma	2 (0.4)	73.5
Transitional cell carcinoma	1 (0.2)	64.0

Table 2. Age Distribution of Benign and Malignant Prostatic Lesions

Age (years)	<40	40-49	50-59	60-69	70-79	80-89	≥90	Total
BPH	2	2	20	56	67	31	1	179 (52.2%)
BPH with inflammation	1	4	13	47	57	30	4	156 (45.5%)
Inflammation		2		4	2			8 (2.3%)
	3 (0.8%)	8 (2.4%)	33 (9.6%)	107 (31.2%)	126 (36.7%)	61 (17.8%)	5 (1.5%)	343 (100%)
Adenocarcinoma		1	6	19	21	22	2	71 (95.9%)
Squamous cell carcinoma					2			2 (2.7%)
Transitional cell carcinoma				1				1 (1.4%)
		1 (1.4%)	6 (8.1%)	20 (27%)	23 (31.1%)	22 (29.7%)	2 (2.7%)	74 (100%)

Benign prostatic hyperplasia (both with and without inflammation) was the commonest prostatic lesion and accounted for 80.3% of all cases and 97.6% of all benign cases. The age range was 20 to 97 years with a mean of 69.2 years and a peak age group at 70-79 years.

Table 2 shows the histological patterns of prostate cancer and their distribution in the various age groups. The majority of the prostatic cancer (n=23; 31.1%) were seen in the age group 70-79 years, followed by 29.7% and 27% of cases seen in the age groups 80-89 years and 60-69 years respectively (Table 2). Adenocarcinoma was the commonest histological subtype and seen in 95.9% of all malignant lesions. Rare histological variants of prostatic cancer encountered in the present study included 2 cases (2.7%) of squamous cell carcinoma and 1 case (1.4%) of transitional cell carcinoma.

Gleason grading of the 71 adenocarcinomas showed that moderately differentiated carcinomas (Gleason score of 5-7) comprised the largest group with 41 cases (57.7%), and poorly differentiated carcinomas (Gleason score of 8-10) was the next most frequently with 26 cases (36.6%); well differentiated cancers with Gleason scores of 2-4 comprised 4 cases (5.6%).

Among the cohort of cancer patients, PSA values were accessible in 65 patients. PSA values ranged widely between 16-1865 ng/ml with a mean of 363.4 ng/ml. Detailed analysis of all patients with available PSA data revealed that one (1.5%) patient had a PSA level of <20 ng/ml, 11 (16.9%) of 20-99 ng/ml and 53 (81.6%) patients had PSA levels of >100 ng/ml. The PSA levels increased with Gleason score. The mean PSA levels for patients with well differentiated carcinomas (Gleason score of 2-4) was 100 ng/ml compared with 210 ng/ml in patients with moderately differentiated carcinomas (Gleason score of 5-7) and 588 ng/ml in patients with poorly differentiated carcinomas (Gleason score of 8-10) (Figure 1). There were no statistically significant differences between the PSA levels in patients with Gleason score of 2-4 compared with Gleason score of 5-7; (p=0.332). However, there were significant differences between the PSA levels in patients with well differentiated carcinomas and patients with poorly differentiated (Gleason score of 8-10) carcinomas (p=0.0304).

Discussion

Prostatic diseases cause a significant morbidity in the older age group males all over the world, BPH being quite common cause of Lower Urinary tract symptoms (LUTS) especially urinary outflow obstruction and nocturia etc. Prostatic carcinoma is being diagnosed more frequently in most of the countries, esp. the western developed countries where screening programs with serum PSA estimation have commenced.

In our eight-year study period, we had a total of 417 prostate specimens. Three hundred and forty-three (82.3%) specimens were benign and seventy four (17.7%) were malignant. Our findings are within the range of the figures reported in recent literature. Benign diseases have been reported to range from as low as 62% of the total number of 220 cases in a Pakistani study (Jaffar et al., 2011) to figures as high as 88.5% of total 1163 cases from Oman (George and Thomas, 2004). This range in case of adenocarcinoma has been reported from as low as 10% cases in KSA (Mansoor, 2002) to the high figures of 28.9% from Nigeria (Anunobi et al., 2011) and 28.5% from KSA (Mosli et al., 2009).

In the benign group, BPH (including BPH with inflammation) was the most common lesion, accounting for 80.3% of the all specimens and 97.6% of all benign lesions. The age range was 20 to 95 years. According to the recent literature, the youngest patient to be diagnosed with BPH was 33 years old (George and Thomas, 2004) and the oldest patient at the time of diagnosis was 100 year old (Mosli et al., 2009). Thus in our observation, now the youngest patient at the time of diagnosis of BPH was 20 year old.

In our present study, the earliest age at diagnosis of CaP was 44 years and the oldest was 95 years with mean age of 71.2 years. Nigerian scientists in their more than 200 cases of CaP, report the youngest age at diagnosis to be 40 years (Anunobi et al., 2011). Very closely, the Omani study reports the youngest patient with carcinoma to be 45 years (George and Thomas, 2004). Mansoor (2002) reported 66.8 years as mean age of presentation in 54 CaP cases from the Western region of KSA. Towards the higher end, in a large study from Greece reporting 1714 new CaP cases during 1999-2010, the mean age at diagnosis was 74 years (Grivas et al., 2012).

Adenocarcinoma was the commonest histological subtype and seen in 95.9% of all malignant lesions. Two cases (2.7%) of squamous cell carcinoma (SCC) and one case (1.4%) of transitional cell carcinoma (TCC) were also diagnosed in our study. All the prostate disease studies in the recent literature have mentioned adenocarcinoma of prostate as the commonest tumor. None of the study recently has mentioned any other malignancy of prostate in their series except the study from Oman, reports two cases Non Hodgkin lymphoma (28 and 80 years old), in their 1163 patients' series (George and Thomas, 2004). SCC is a rare tumor of prostate with aggressive behavior. The recent literature search reveals only an occasional case review (Malik et al., 2011) or case report (Wang et al., 2012). Prostatic involvement by TCC is not uncommon and can occur as primary TCC with foci of Carcinoma in-situ or as extension from Bladder TCC (Huguet, 2012).

Regarding the grading of adenocarcinoma, due the local practices and retrospective nature of study, both the older and newer classification has been used i.e. the older classification of differentiation (well, moderate and poor) and the newer classification of Gleason scoring system. In summary, moderately differentiated carcinomas (Gleason score of 5-7) was the most frequently diagnosed carcinoma accounting for 57.7% (n=41) of all adenocarcinoma cases. In our study, Gleason score seven was the most frequent (39.4%). In the recent literature, Gleason score 6 was found to be the commonest by Greek and Jamaican researchers (Grivas et al., 2012; Anderson-Jackson et al., 2012); while Gleason score 7 was found to be the commonest by Malaysian and another group of Pakistani workers (Hong et al., 2010; Arshad and Ahmad 2013). On the contrary, another group from Pakistan have reported

well differentiated carcinoma (Gleason score 2-4) as the most frequent in their study (Hameed et al., 2010). Two studies have found poorly differentiated carcinoma (Gleason 7 to 10) as most frequent (George and Thomas, 2004; Anunobi et al., 2011). The recent KSA study report mainly moderate to poorly differentiated adenocarcinoma (Gleason 6 and above) as the most frequent (Mosli et al., 2009).

In the 65 CaP patients, where Prostate-Specific Antigen (PSA) values were available, majority (81.6%) had PSA >100 ng/ml, which increased with Gleason score. Anunobi et al. (2011), from Nigeria report PSA levels above 50ng/ml were only present in malignant cases. A group from Jamaica also report that the PSA levels increased with higher Gleason scores (Anderson-Jackson et al., 2012). Two groups from KSA had similar observation; first group in 2003 observed that when PSA was elevated to 4-10 ng/ml TRUS guided biopsy detected cancer in 21.4%, while elevation of PSA to 10-20 ng/ml lead to cancer detection in 40% of the patients, and when PSA was above 20 ng/ml all cases were positive for cancer (Tayib et al., 2003). Recently the second group of researcher found that PSA values <4 ng/ml were found in 13.6% of PCa patients and supported the recommendations to lower the PSA cutoff value for prostatic biopsy to 2.5 rather than 4 ng/ml (Mosli et al., 2009).

In our study, a statistically significant difference was found in the PSA levels between well differentiated and poorly differentiated carcinomas (p=0.0304). Statistical analysis and P values comparing PSA and Gleason scores were available in two recent studies. Coard and Skeete (2008), conclude in their large study confirmed that there was a statistically significant positive and moderate correlation between serum PSA level and Gleason score (Spearman r 0.49; p<0.001). In the Greek study by Grivas et al. (2012), a positive correlation was found between Gleason score and PSA (p=0.013).

In conclusion, prostatic diseases in Madinah region of KSA have the same pattern and demographics as reported in the recent international literature for the world population as well as for region of Middle East and KSA. We were able to demonstrate statistically significant positive correlation between PSA levels and differentiation of Adenocarcinoma, therefore recommend screening programs utilizing use of blood PSA levels in the older male population of KSA, for the early detection of CaP.

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