Clinicopathological Spectrum of Prostatic Adenocarcinoma in 60 Patients

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Abstract

Background: Prostatic adenocarcinoma represents the second most common malignant tumor found in men over 65. It constitutes a source of morbidity and mortality.

Methods: Haematoxylin and Eosin-stained-slides of sixty archival formalin fixed paraffin-embedded, routinely processed cases (30 cases as TUR-P biopsies, 26 cases as radical prostatectomy specimens and 4 cases as open prostatectomy specimens) were retrospectively and randomly collected from the Department of Pathology, Kasr El-Aini Hospital, Cairo University.

Results: Seventy percent of patients aged above 60 years (the mean age was 67.38). Twenty-five patients (41.7%) had preoperative serum PSA level more than 10 up to 20ng/ml. Histologically, the acinar pattern was the most prevalent (29%). The majority (56.7%) had high-grade tumors. Perineural invasion was detected in 22 cases while 11 showed positive capsular invasion. In the 26 radical prostatectomy cases, the disease was confined to the gland (pT2) in 18 patients (69.3%) however; the remaining eight patients (30.7%) were staged as pT3.

Conclusion: Serum PSA level does not significantly correlate with pathological features of prostatic adenocarcinoma. On the contrary, perineural invasion in radical prostatectomy is strongly associated with tumor grade and stage.

Key Words: Prostatic adenocarcinoma – PSA – Gleason score.

Introduction

PROSTATE cancer is the most common male genital cancer. Among blacks, it has been described as a public health epidemic. Other than skin cancer, prostate cancer is the most common cancer in American men. It is the second leading cause of cancer death, behind only lung cancer [1]. In 2015, the American Cancer Society estimated over 220,000 men were newly diagnosed with prostate cancer and more than 27,800 men died from the disease though many of them had lived with the disease for years prior to their deaths [2].

Prostatic Adenocarcinoma (PCa) accounts for about 95% of prostatic neoplasms and it represents the second most common malignant cell growth found in men over 65. According to the National Cancer Institute, Cairo University, it has been reported in 95.74% of cases with prostatic tumors during the period 2003-2004 [3,4]. Currently, most cases of prostate cancer are found because of abnormalities in a screening PSA level or findings on Digital Rectal Examination (DRE) rather than because of symptoms. However, prostate cancer can be an incidental pathologic finding when tissue is removed during transurethral resection (TUR-P) to manage obstructive prostatic symptoms [5].

Men who have first-degree family members with cancer prostate are at higher risk of getting the disease compared to men without family history [6]. Mutations in BRCA1 and BRCA2 have also been implicated in prostate cancer. Other linked genes include the Hereditary Prostate cancer gene 1 (HPC 1), the Androgen Receptor (AR), and the vitamin D receptor [7].

Histologically, prostatic carcinoma can be classified into acinar and non-acinar types. The non-acinar group accounts for about 5-10% of carcinomas that originate in the prostate [8].

The Gleason grading system is clearly the most widely accepted. It assigns a grade using numbers from 1 to 5 based on the glandular and cellular pattern of the tumor as evaluated at relatively low magnification [9]. Meanwhile, the stage is based on the prostate biopsy results including the Gleason sum, the PSA level, and any other exams or tests.
to find out how far the cancer has spread. In both staging and grading, the higher the numbers the worse the news [10]. In general, prostate cancer is often a slow moving disease and actually has a very high survival rate. According to the most recent data, when including all stages of prostate cancer: The 5-year relative survival rate is almost 100%, the 10-year relative survival rate is 98% and the 15-year relative survival rate is 95% [11].

The aim of work was to evaluate different histological patterns of prostatic adenocarcinoma, Perineural Invasion (PNI), and capsular invasion, grading and staging in radical prostatectomy specimens and to correlate these histopathological data with clinical variables as age and serum PSA level.

Material and Methods

Sixty archival formalin fixed paraffin-embedded, routinely processed cases (30 cases as TUR-P biopsies, 26 cases as radical prostatectomy specimens and 4 cases as open prostatectomy specimens) were retrospectively and randomly collected from the Pathology Department, Kasr El-Aini Hospital, Cairo University (January 2011-December 2012). For each collected case, the following clinical data could be retrieved from the computer files including; age of the patient, PSA level and Tumor Node Metastasis (TNM) stage in cases of radical prostatectomy. Serial sections from each tissue block were cut at 5 microns thickness and was stained by Haematoxylin and Eosin (H & E), for histopathological evaluation. Sections were re-evaluated by two independent pathologists. Tumor grade was determined according to modified Gleason grading system, 2005 [12].

Statistical analysis:

Fisher exact and chi-square tests were used in the analysis. The significance of the results was assessed by determining the probability factor “p” value. p-value of <0.05 was considered significant.

Results

In this study, the mean age of prostatic adenocarcinoma patients was 67.38 (ranging between 38-88 years), with a count of 42 cases (70%) above the age of 60. The available preoperative serum PSA level ranged from 4 up to 115ng/ml with a mean 29.58. For statistical analysis, serum PSA level was categorized into five groups (<10), (10-<20), (20-<40), (40-<80) and (>80). It was found that, the highest number of patients (25 representing 41.7%) had serum PSA level more than 10 up to 20ng/ml. Various morphological patterns could be noticed include glands (29%), cribriform (13.3%), hypernephroid (11.7%), solid sheets (8.3%) and comedonecrosis (3.3%) (Table 1) & Fig. (1A,B).

Table (1): Distribution of cases according to presence of special morphological pattern.

<table>
<thead>
<tr>
<th>Valid:</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional (glands)</td>
<td>29</td>
<td>48.3</td>
</tr>
<tr>
<td>Cribriform</td>
<td>8</td>
<td>13.3</td>
</tr>
<tr>
<td>Cribriform + comedonecrosis</td>
<td>2</td>
<td>3.3</td>
</tr>
<tr>
<td>Glomeruloid</td>
<td>1</td>
<td>1.7</td>
</tr>
<tr>
<td>Hypernephroid</td>
<td>7</td>
<td>11.7</td>
</tr>
<tr>
<td>Mucin activity</td>
<td>4</td>
<td>6.7</td>
</tr>
<tr>
<td>Solid sheets</td>
<td>5</td>
<td>8.3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>60</strong></td>
<td><strong>100.0</strong></td>
</tr>
</tbody>
</table>

Fig. (1): (A) Prostatic adenocarcinoma Gleason grade 3 showing irregular malignant glands infiltrating in between the normal glands. (B) Intraluminal cribriform proliferation (H & E X100).
Gleason grade 4 was the most common grade among the collected cases (32 cases representing 53.3%) while, grade 2 was the least common (only 3 cases representing 5%). The mean Gleason Score (GS) was 7.83 with a higher frequency for GS 9 (21 cases; 35%) Fig. (2) distributed as 15 cases with Gleason grade (4+5) and 6 cases with Gleason grade (5+4). Gleason score 7 was the second most common (18) cases; 11 cases had Gleason grade (3+4) and 7 cases had Gleason grade (4+3). GS 5 as well as GS 10 showed the lowest frequency; only three cases for each. For statistical analysis, the tumors were considered well differentiated when GS was ≤6, and moderately differentiated when the GS was 7 and poorly differentiated when the GS was 8 to 10.

Over all, Perineural Invasion (PNI) was detected in 22 cases (18 out of which were radical prostatectomies) and absent in 38 cases (63.3%) Fig. (3,4A). 11 cases (18.3%) out of 60 cases [distributed as 9 radical and 2 open prostatectomy specimens] showed positive capsular invasion by tumor tissue Fig. (4B).

In the 26 radical prostatectomy cases, the disease was confined to the gland in 18 patients (69.3%) staged as pT2 (A, B, C). The tumor extended beyond the prostate; stage pT3 (A, B) in the remaining 8 patients (30.7%). Lymph nodes were excised bilaterally in 23 cases with positive metastases in 4 cases having lymph node stage N1; 3 cases of which showed tumor stage T3b and stage T2c in one case.

We found significant statistical relationship between the age and GS (p-value=0.043), perineural invasion and GS in radical prostatectomy cases (p-value=0.006) (Table 2) as well as perineural invasion and the pT stage (p-value <0.005) (Table 3).

On the other hand, the correlation between preoperative serum PSA level and other pathological features as tumor grade and GS Fig. (5) revealed no statistical significance (p-value=0.251 and 0.236, respectively). Additionally, there was no correlation between pathologic T stage and GS in radical prostatectomy cases (p-value=0.587) (Table 4).
Table (2): Correlation between perineural invasion and Gleason score in the 26 radical prostatectomy specimens.

<table>
<thead>
<tr>
<th>Gleason score</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>GS 7</td>
<td>4</td>
</tr>
<tr>
<td>GS 8-10</td>
<td>3</td>
</tr>
<tr>
<td>GS 8-10</td>
<td>1</td>
</tr>
<tr>
<td>GS 8-10</td>
<td>8</td>
</tr>
</tbody>
</table>

**Perineural invasion:**
- **Negative:**
  - Count: 4
  - % of total: 15.4%
- **Positive:**
  - Count: 3
  - % of total: 11.5%

**Total:**
- Count: 5
- % of total: 19.2%

\(p\)-value=0.006.

Table (3): Correlation between pT stage and PNI in the radical prostatectomies.

<table>
<thead>
<tr>
<th>PNI</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>pT2a</td>
<td>3</td>
</tr>
<tr>
<td>% of total</td>
<td>11.5%</td>
</tr>
<tr>
<td>pT2b</td>
<td>2</td>
</tr>
<tr>
<td>% of total</td>
<td>7.7%</td>
</tr>
<tr>
<td>pT2c</td>
<td>6</td>
</tr>
<tr>
<td>% of total</td>
<td>23.1%</td>
</tr>
<tr>
<td>pT3a</td>
<td>1</td>
</tr>
<tr>
<td>% of total</td>
<td>3.8%</td>
</tr>
<tr>
<td>pT3b</td>
<td>6</td>
</tr>
<tr>
<td>% of total</td>
<td>23.1%</td>
</tr>
</tbody>
</table>

**Total:**
- Count: 18
- % of total: 69.2%

\(p\)-value <0.005.

Table (4): Correlation between pathologic T stage and Gleason score in radical prostatectomy cases.

<table>
<thead>
<tr>
<th>Gleason score</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>GS 7</td>
<td>3</td>
</tr>
<tr>
<td>GS 8-10</td>
<td>2</td>
</tr>
<tr>
<td>GS 8-10</td>
<td>2</td>
</tr>
<tr>
<td>GS 8-10</td>
<td>7</td>
</tr>
</tbody>
</table>

**Tumor stage:**
- **pT2a:**
  - Count: 3
  - % of total: 11.5%
- **pT2b:**
  - Count: 0
  - % of total: 0%
- **pT2c:**
  - Count: 1
  - % of total: 3.8%
- **pT3a:**
  - Count: 1
  - % of total: 3.8%
- **pT3b:**
  - Count: 0
  - % of total: 0%

**Total:**
- Count: 18
- % of total: 69.2%

\(p\)-value=0.587.

**Discussion**

The most important and established indicators of prognosis for prostate carcinoma include the Gleason grade, the extent of tumor volume, and the presence of capsular penetration or margin positivity at the time of prostatectomy [13].

In our cohort, the mean age of prostatic adenocarcinoma patient was 67.38 (ranging 38-88 years). Seventy percent of cases aged above 60 years. This is very close to results shown by Baek et al., [14]. However, it is much higher than that reported by Fonseca et al., [15] who found that the mean age was 62 years (range 41-75). These differences might be due to the variability in sample sizes with different ranges of ages.

Morphologically, we found that the acinar pattern of prostatic adenocarcinoma was the most prevalent (48.3%) followed by the intraluminal cribriform growth pattern (16.6%). Comedonecrosis
as well as glomeruloid patterns were the least common (3.3% and 1.7%, respectively). This is comparable well with a study done by Garg et al., [16].

The majority (56.7%) had high-grade adenocarcinomas (GS 8-10), followed by moderately differentiated tumors (30%). This is similar to that reported by Catalona et al., [17] and Obiorah and NWOSU [1]. On the contrary, Zivković [18], Hussain et al., [19] and Forae & Aligbe [20] stated that moderately differentiated prostatic adenocarcinoma with (GS 5-7) was the most predominant type.

Studying the correlation between preoperative serum PSA level and other pathological features as tumor grade and Gleason score revealed no statistical significance (p-value=0.251 and 0.236, respectively). This goes to that reported by Sithininamsuwan et al. [21]. However, it sharply contrasts with studies done by Zivković [18] and Kankaya et al., [22], which showed a highly positive correlation between serum PSA and Gleason grade.

Many factors can influence the accuracy in determination of serum PSA level like using different laboratory equipments, immediate manipulation on prostate (DRE, prostate massage, endoscopic examination) before taking a blood sample for PSA and presence of associated prostatic lesions (severe prostatitis, infarction and PIN). The aforementioned factors as well as variation in the scoring systems might explain this difference in results.

PNI was identified in 18 out of the collected 26 radical prostatectomy specimens. Most specimens with positive PNI were found to be associated with higher-grade tumors (p-value=0.006) and advanced T stage (p-value <0.005). These results are consistent with studies done by Ng et al., [23], Cambruzzi et al., [24] and Nzioka and Onyuma [25].

PNI is a well-known risk factor in other malignancies. Contact with nerves may confer a survival advantage for cancer cells, as in experiments, malignant prostate cells show enhanced proliferation and decreased apoptosis in culture with nerves [26]. The clinical significance of PNI is controversial. Loeb et al., [27] showed that PNI in a prostate biopsy is an independent risk factor for aggressive pathological features and a non-independent risk factor for biochemical progression after radical prostatectomy.

**Conclusion:**

Prostatic adenocarcinoma is a disease of elderly men, although young men are not excluded. Most patients present late with high GS carcinoma. Serum PSA level does not correlate with pathological features of the tumor. On the other hand, perineural invasion in radical prostatectomy is strongly associated with tumor grade and stage.

**References**


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