DIFFERENT MODALITIES IN DIAGNOSIS AND TREATMENT OF ADVANCED PROSTATIC CARCINOMA

Essay submitted for partial fulfilment of

Master Degree in urology

Presented by

Mokhtar Abdel-Salam Metawea

Under the supervision of

Prof Dr. Ismail Osman Abdel-Hafiz

Professor of urology

Ain Shams University

Dr. Ahmed Salah Hegazy

Lecturer of urology

Ain Shams University

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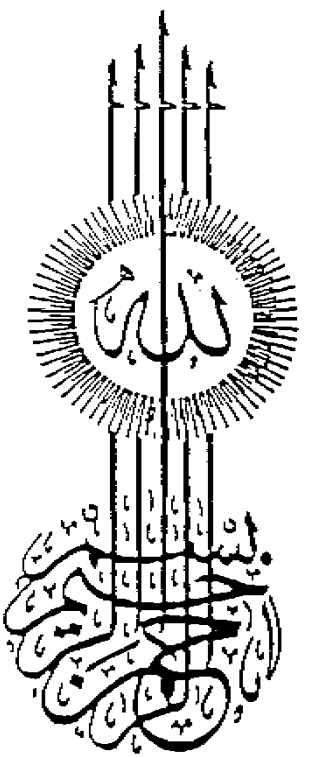

قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا
عَلَّمْتَنَا إِنَّكَ أَنْتَ الْعَلِيمُ الْحَكِيمُ .

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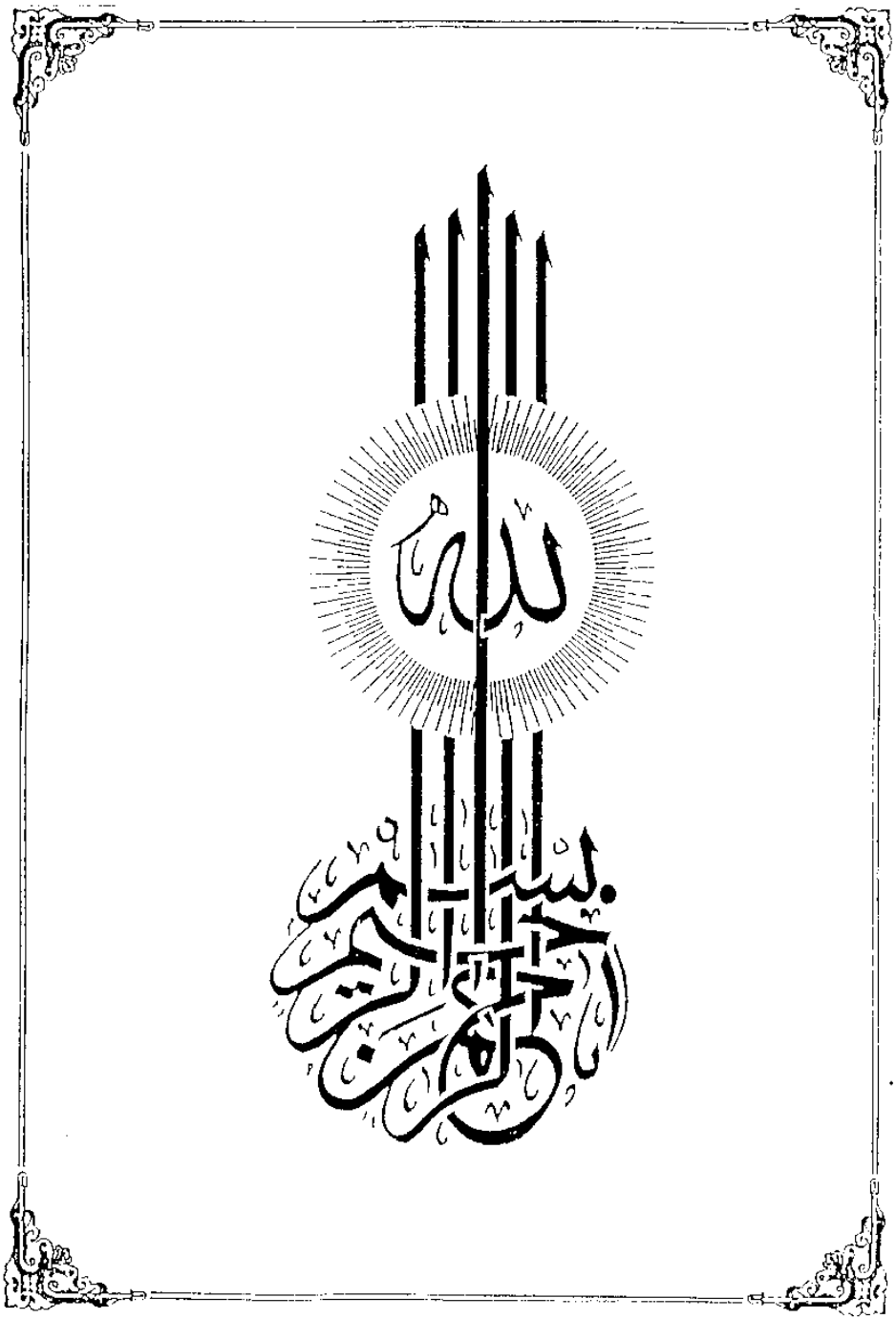

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Introduction

INTRODUCTION

In spite of recent advances in the ability to diagnose prostate cancer, the majority of patients found to have this disease have advanced cancer at the of time detection. Adenocarcinoma of the prostate is the most common cancer among American men and will account for 20% of newly diagnosed cancer, and 11% of male cancer deaths in 1990. Advanced stage disease (C, D_0, D_1, D_2, D_3) will be identified in more than 40% of these cases **(Silverberg et al., 1990).**

About 60% of patients with untreated stage C disease will exhibit evidence of disease progression at 5 years, with annual progression rates of 10% to 12% being anticipated. About 85% of patients with stage D1 disease demonstrate progression within 5 years and those with distant metastases (stage D_2) have a median survival of about 30 months with an anticipated 5 years survival rate of approximately 20% **(Geller et al., 1984; Crawford et al., 1989).**

ANATOMY OF THE PROSTATE

The prostate gland is classically described as a compressed inverted cone surrounding the very beginning of the male urethra. It lies behind the pubic symphysis, separated from it by a rich plexus of veins (**Santorin's plexus**) and some loose adipose tissue. Near its apex it is connected to the pubic bone by the puboprostatic ligaments. Posteriorly it is related to the ampulla of the rectum, separated from it by its own capsule and by Denonvilliers' fascia. Superiorly it is continuous with the bladder neck. Inferiorly, the apex of the prostate is lying on the superior aspect of the superior fascia of urogenital diaphragm. The inferolateral surfaces are prominent and are related to the anterior part of the levator ani muscles which are separated from the gland by a rich plexus of veins.

Lymphatic drainage of the prostate:

The primary lymphatic drainage from the prostatic gland goes to the external and internal iliac groups as well as to the obturator lymph nodes. Lymphatics from all these sites congregate and join the common iliac lymph nodes

Blood supply of the prostate:

The main blood supply to the prostate is from the inferior vesical artery which penetrates the substance of the prostate at the prostatovesical junction at about 4 and 8 O'clock positions. Although there are veins accompanying these arteries, these veins join to form a very rich venous plexus situated between the prostate and the prostatic sheath. This venous plexus has free communication with the inferior hypogastric venous system as well as the presacral prevertebral venous plexus.

Histology of the prostate:

It is a fibromuscular glandular organ that surrounds the prostatic urethra. The glandular component of the prostate consists of ducts which branch out from the urethra and terminate into acini. The proximal portions of the prostatic ducts are lined by transitional epithelium similar to the urethra. In distal portions of the prostatic ducts as well as in scattered prostatic acini are most commonly lined by tall columnar epithelium, this columnar epithelium has pale staining granular cytoplasm and is called secretory epithelium, it contains enzymes that stain abundantly with prostatic specific antigen, acid phosphatase, and other enzymes such as leucine aminopeptidase.In androgen ablation,

the typical secretory cells decrease by 90% in total number, become cuboidal, and shrink by 80% in cell volume and 60% in cell height **(Deklerk et al., 1976)**. Situated beneath the secretory cells, is the basal cell layer which has scant cytoplasm and oval nuclei, the plasma membrane is rich in ATPase suggesting that these cells may be involved in active transport, also it is believed that these basal cells give rise to secretory epithelial cells as a type of stem cell **(Merk et al.,1982)**. It is important to distinguish it from surrounding fibroblast, recognition of the basal cell layer is important since it is not present in adenocarcinoma of the prostate and may be identified in many conditions which mimic prostate adenocarcinoma. Neuro-endocrine cells are found in the epithelium of the acini and in ducts of all parts of the gland as well as in the prostatic urethra. There are three types of prostate neuroendocrine cells with the major type containing both serotonin and thyroid stimulating hormone, the two minor cell types contain calcitonin and somatostatin **(Abrahmsson and Lilja, 1989)**. It is most probable that these neuroendocrine cells may be involved in regulation of prostatic secretory activity and cell growth. The fibromuscular element of the prostate is directly continuous with the muscular element of the smooth musculature of the bladder neck. This fibromuscular stroma condenses on the periphery of the gland to form the

total glandular tissue of the prostate. Almost all carcinomas arise in this region. Furthermore, this is the tissue sampled in most random biopsies of the prostate.

3- Central zone:

It surrounds the ejaculatory ducts completing the proximal quadrant of glandular tissue above and behind the vermontanum. It makes up about 25% of the prostatic functioning glandular tissue. The acinar tissue of the central zone consists of large spaces of irregular contour, with numerous ridges projecting into the lumen, the epithelial cells are crowded with large nuclei. This is an uncommon zone for origin of carcinoma of the prostate.

4- Preprostatic tissue:

This constitutes less than 1% of the mass of the glandular prostate, it surrounds the anteriorly displaced urethra proximal to the upper end of the verumontanum.

5- Transitional zone:

It is located just outside the urethra at the verumontanum. It makes up less than 5% of the mass of the normal glandular prostate. It is the exclusive site of origin of benign prostatic hyperplasia.

CLASSIFICATION OF PROSTATE CANCER BY CELL TYPE OF ORIGIN

* **PRIMARY:**

I- Epithelial:

A) Adenocarcinoma:

* Parent epithelium: secretory lining of duct branches and acini
* Patterns: Cribriform, papillary, undifferentiated endometrioid, mucinous and cystadenocarcinoma.

B) Transitional cell carcinoma:

* Parent epithelium: Prostatic urethra, major trunk ducts in proximity to urethra, metaplasia (ischemic or inflammatory) in duct branches and acini.
* Patterns: Intraductal, transitional cell carcinoma, invasive transitional cell carcinoma.

C) Squamous cell carcinoma:

* Parent epithelium: In squamous metaplasia of prostatic urethra.

D) Neuroendocrine carcinoma:

* Parent epithelium: Serotonin cells of duct branches and acini.
* Patterns: Often mixed

- Adenocarcinoma with neuroendocrine peptides.
- Carcinoid tumour.
- Small cell (oat cell) carcinoma.

E) Undifferentiated carcinoma:

II- <u>Stromal</u>:

Rare, wide variety of types known as sarcomas.

A) Rhabdomyosarcoma:

Most patients are younger than 10 years.

B) Leiomyosarcoma:

Most patients are older than 40 years.

C) Others (fibrosarcoma, histiocytomas).

* **<u>SECONDARY</u>:**

A) Direct invasion from bladder:

Transitional cell carcinoma.

B) Direct invasion from colon adenocarcinoma:

Uncommon.

C) Metastasis:

Seeding from widely disseminated cancer; rare; lung, 50%; melanoma, 35%.

D) Lymphoma:

Rare.

Staging of Prostatic Cancer:

I) **In staging system proposed by Whitmore (1965), tumours are categorized as follows:**

Stage A:

Tumours are microscopic and intracapsular, and detected by microscopic examination of prostatic tissue removed for B.P.H. It is further subdivided into A_1(Focal),A_2 (diffuse).

* A_1 is diagnosed when less than 5% of the specimen is cancerous and of well or moderate differentiation.
* A_2 is that in which more than 5% of the tissue is malignant and/or highly anaplastic.

Stage B:

Tumours are macroscopic and intracapsular.

* B_1: Tumours occupying 1 lobe and less than 1.5 cm in size.
* B_2: Tumours occupying 2 lobes or more than 1.5 cm in size.

Stage C:

Tumours are macroscopic and extracapsular.

* C_1: minimal periprostatic invasion with no involvement of seminal vesicles.
* C_2: Involvement of seminal vesicles and/or ureteric obstruction.

Stage D:

Metastatic disease:

* D_0: Patients with localized tumour, a normal bone scan but persistently elevated acid phosphatase.
* D_1: Patients with stages A, B or C who are found to have lymph node involvement.
* D_2: Patients with evidence of distant metastasis in bones or elsewhere.
* D_3: Patients with D2 who received endocrine therapy but have relapsed.

II- TNM classification of prostatic carcinoma:

Primary tumour (T):

* TX: Anatomic relationships indefinable (e.g, prior total prostatectomy).

* TA: Digitally unrecognizable cancer (confirmed histologically and substaged if traditional TUR cancer).

  TA_1 ≤ 5% of total surgical specimen and of low to medium grade.

  TA_2 > 5% of specimen, any grade, or ≤ 5% of specimen with any high grade.

  TAX TA, but not A1 or A2.

  TAX-TRUS Detected by ultrasound, confirmed by biopsy.