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شبكة المعلومات الجامعية

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التوثيق الالكتروني والميكروفيلم

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بالرسالة صفحات
لم ترد بالأصل

DRUG THERAPY IN CANCER PROSTATE

ESSAY
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INTRODUCTION

Prostatic cancer is now the most common malignant disease affecting men, and it is the main cause of cancer deaths in men over age fifty.

Thus prostate cancer is not only a clinical problem, but is of major socioeconomic importance.

Unfortunately, owing to lack of early symptomatology and the law specificity of the diagnostic tools prosently available, the majority of patients have locally advanced or metastatic disease at the timt of diagnosis.

However, if the disease is discovered when it is still confined to the prostate, radical prostatectomy is curative, and is associated with only minimal or absent mortality and acceptable morbidity.

For patients with locally or regionally advanced or metastatic prostate cancer, androgen ablation has been the mainstay of treatment for over four decades. Initially, suppression of levels of circulating androgens was achieved by administration of estrogens or by bilateral orchiectomy. The main side effects are in the form of thromboembolic manifestations and psychic trauma.

The advent of new therapeutic modalities allows us now to overcome this problem, the first major advance was the development of LH-RH analogues as well as the anti-androgens. However, they carry a great risk to the patient. For hormone resistent prostatic cancer patients chemotherapeutic agents may be benificial.

For completion, other therapeutic modalities are encountered as immunotherapeutic drugs and cryotherapy.

The aim of our work is to evaluate the role of drug therapy in the management of cancer prostate. The time factor, combination element and the stage of the disease will be taken in consideration.

A comparison between drug therapy and other lines of therapy will came into view.

Anatomy of the prostate

This glandular organ lies beneath the bladder and above the urogenital diaphragm,and is penetrated by the proximal part of the urethra. It is normally broader than it is long , approximately 4*3*2 cm , and roughly the size shape of a chestnut.

It is clasped on each side by the levator prostate part of levator ani, The Prostate provides about 20% of the volume of seminal fluid .

THE PROSTATE has a base and an apex , and anterior , posterior and inferolaterel surfaces.

THE base is the upper surface , fused with the neck of the bladder and perforated by the urethra which traverses the whole length of the gland.

THE blunt apex is the lowest part , and the prostatic urethra emerges from the front of the apex to become the membranous urethra which penetrates the urogenital diaphragm.

THE anterrior surface is at the back of retropubic space and is connected to the bodies of the pubic bones by the puboprostatic ligaments. the inferolateral surfaces are clasped by the levator prostate parts of levator ani , while the posterior surface, which has a vertical median groove palpable in rectal examination, is in front of the lower rectum but separated from it by the rectovesical fascia. the ejaculatory duct pierce the posterior surface just below the bladder and pass obliquely through the gland for about 2 cm to open into the prostatic urethra about half way down . The prostate own duct also open into this part of the urethra.

A thin layer of connective tissue at the periphery of the gland forms the true capsule of the prostate and outside this there is a condensation of pelvic fascia forming the false capsule between these two capsule lies the prostatic plexus of veins .

A THIRD or pathological capsule is described when tumor tissue compresses normal surrounding part , if benign, the growth can be shelled out from this compressed capsule.

[MCNeal,J'E 1981]

Lobes and structures

THE gland consists of acini of varying shape and sizes embedded in a fibromuscular stroma-a mixutre of connective tissue and smooth muscle, this is the characteristic histilogical feature, numerous small prostatic duct open into the prostatic urethra.

IT is customary to consider the gland as being made of five lobes- anterior, middle, posterior and two lateral lobes- but there is usually no clear distinction between them. THE anterior lobe is the small area in front of the Urethra, it is unimportant, consisting almost entirely of stromal tissue with few acini. THE middle lobe is the region between the ejaculatory ducts and the proximal urethra , and is of great importance's since , when affected by benign hypertrophy. it elongates and obstructs the urethra .

Minor degrees of hypertrophy of this lobe without urethras abstraction cause as small swelling at the apex of the Trigon of the bladder . the rest of the gland at the back and side forms the combined posterior and lateral lobes , which are best regarded simply as right and left lobe.and again are important not only because of simple enlargement but as the commonest sites of cancerus change. Enlargement of the lateral lobes may be detected on rectal examination but middle lobe enlargement extending forwards into the bladder will not be .

Benign hypertrophy of the prostate is usually not a generalized enlargement but a local adenomatous proliferation in the internal zone or central region of any of the lobes adjacent to the urethra - the region of the so-called mucosal or periurethral glands.

THE acini is the much larger outer or peripheral zones of any lobe are the ones affected by carcinoma.

THE PROSTATIC URETHRA extend from the internal urinary meats to the apex of the prostate and is the widest part of the urethra. IT is characterized posteriorly by a midline longitudinal ridge, the urethral crest or verumontanum. IN the center of this crest is a minute depression, the prostatic utricle, an embryological remnant resulting from union of the caudal ends of the paramesonephric ducts; it is thus the homologue of the female uterus.

A Lengside it , on the urethral crest , the jaculatory ducts open . THE prostatic ducts open on the crest and in the sulcus on each side.

[Hutch,Etal 1970]

BLOOD SUPPLY:

THE main arterial supply is from the prostatic branch of the inferior vesical artery , with some small branches from the middle rectal and internal pudendal vessels passing to the lower part. but sometimes the middle rectal provides the major supply . THE veins run into a plexus between the true and false capsules and this joins the vesicoprostatic plexus situated at the front and sides of the groove between bladder and prostate. At the front , this plexus receives the deep dorsal vein of the penis, and drains backwards into the internal iliac veins.

[Dodds , ETAL 1981]

LYMPH DRAINS:

the lymphatic of the prostate pass across the pelvic floor to internal iliac and sacral nodes but some may reach external iliac nodes.

(Last,1990)

NERVE SUPPLY:

the acini receive parasympathetic (cholinergic) innervation from pelvic splanchnic nerves, but this is mush less important than the muscle fibres of the stroma which contract to empty the glands during ejaculation and which are under sympathetic (adranergic) control from the inferior hypo gastric plexus. **[Young ,Etal 1980]**

Embryology of the prostates:

The prostate gland is formed in embryonic life by a number of evaginations from the posterior and lateral walls of the posterior urethra .

Embryologically , the male prostate is divided into five lobes; the posterior lobe, which is posterior to the urethra and deferential canal;The middle lobe , which lies between the Urethra and the defrential canal, the two lateral lobes , which lie on either side of the urethra and the ducts of which empty into the sides of the verumontanum , and the anterior lobe , a vestigial structure represented by 8 to 10 acini , anterior to the urethra. The ejaculatory ducts pass downward and forward between the middle and posterior lobes.

In the female, the prostate remains vestigial, it corresponds only to the lateral and middle lobes of the male prostate and lacks a posterior lobe . This fact is of interest in relation to nodular hyperpalsia and prostatic carcinoma. The former involves only the ambisexual part of the male prostate , while the latter is predominantly a disease of the posterior lobe, or purely male part of the prostate **(Fisher , 1985)** .

ETIOLOGICAL FACTORS OF CANCER PROSTATE

IN spite of its numerical importance , relatvely little is known about the etology of cancer prostate age ,race , hormones , sexual activity and marital status , diet , occupation , genetic factors , sexually trans mitted infections , plus benign prostatic hyperplasia are some of the proposed etiologic factors of cancer prostate.

I-AGE

Prostatic cancer is a disease of old age.its incidence increases with age and has no peak age incidence ; the older the man becomes the greater the risk.

detailed autopsy studies have demonstrated that approximately 12% of men between 60 and 69 years of age harbor prostatic carcinoma; this percentage increases up to 18% in 70 to 79 years old age group and to 26% in those patients older than 80 years.

(Hanks,et al.,1993)

II-RACE

the highest incidence rates are observed among blacks in USA , reaching up to 100.2 for Alameda blacks , followed by whites in north america e.g. 44.5 for Alameda whites and 28.1 for canadians and the scandinavia 44.4 in sweden.

Incidence rates are intermediate in Europe , being higher in western e.g. 25.7 in France and 18.1 in England than in southern and Eastern Europe e.g. 11 in Poland and Checkoslovakia 8.1 lowest rates are observed in countries of south east Asia e.g. 3.4 in japan and 0.8 in china .

IN AFRICAN blacks, the incidence rates are of the same order as western Euope

RACE AND MORTALITY RATES :

the highest mortality rates are to be found in caribbean countries , unfortunately, countries from which no incidence statistics are available.

the available statistics in prostatic cancer incidence and mortality are based on the sum of clinically diagnosed carcinomas and those latent tumors found unexpectedly at prostatectomy or autopsy.

(Hanks, et al, 1993)

III- SEX HORMONES

sex hormones have been implicated in etiology of cancer prostate primarily on the bases that:-

1. THE grouth and development of this organ requires the presence of sex hormones.
2. THE discovery of steroid hormones receptors in prostatic cancer cells as evidence by the success of estrogen treatment of cancer prostate patients .
3. ALSO , by the fact that it is possible to induce prostatic cancer in experimental animals by prolonged adminestration of male sex hormones .
4. FINALLY , it has been shown that the levels of testosterone and dihydrotestosterone (DHT) are higher in neoplastic prostate tissue than the normal prostatic tissue , as is the uptake of testosterone and its conversion to DHT

however , evidence for correlation studies does not indicate difference in hormone profiles of high and low-risk populations

the results of clinical obeservation studies ,in which comparisons are made between serum levels of different hormones among patients with prostatic carcinoma and healthy controles , are conflicting and difficult to interpret. (Waymont and et al., 1993)

IV SEXUAL ACTIVITY :

sexual activity , which is merely an indicator or indirect measure of hormonal status , has been related to the accurence of cancer prostate.

prostatic cancer patients seam to have a greater sexual drive than controls , but are less sexually active.

According to Rotkin , prostatic cancer patients experience both puberty and first intercourse at a later age than controls

Prostatic cancer mortality rates , are associated with marital status , increassing in the following order:

single , married , widowed , divorced.

it has also been suggested that , among married men the riske is higer in those with children than among those without children

(Rotkin ,1971)