STEROID HORMONE RECEPTORS IN GYNECOLOGIC TUMORS

Essay

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by

Hamdy Mahomed Edries

M.B.,B.CH.

Under supervision of

Prof. Dr. Ibrahim Yassin Abousenna

Professor of Obstetrics and Gynecology

Faculty of Medicine

Ain Shams University

Dr. Mohamed Aly Mohamed Ibrahim

Lecturer of Obstetrics and Gynecology

Faculty of Medicine

Ain shams University

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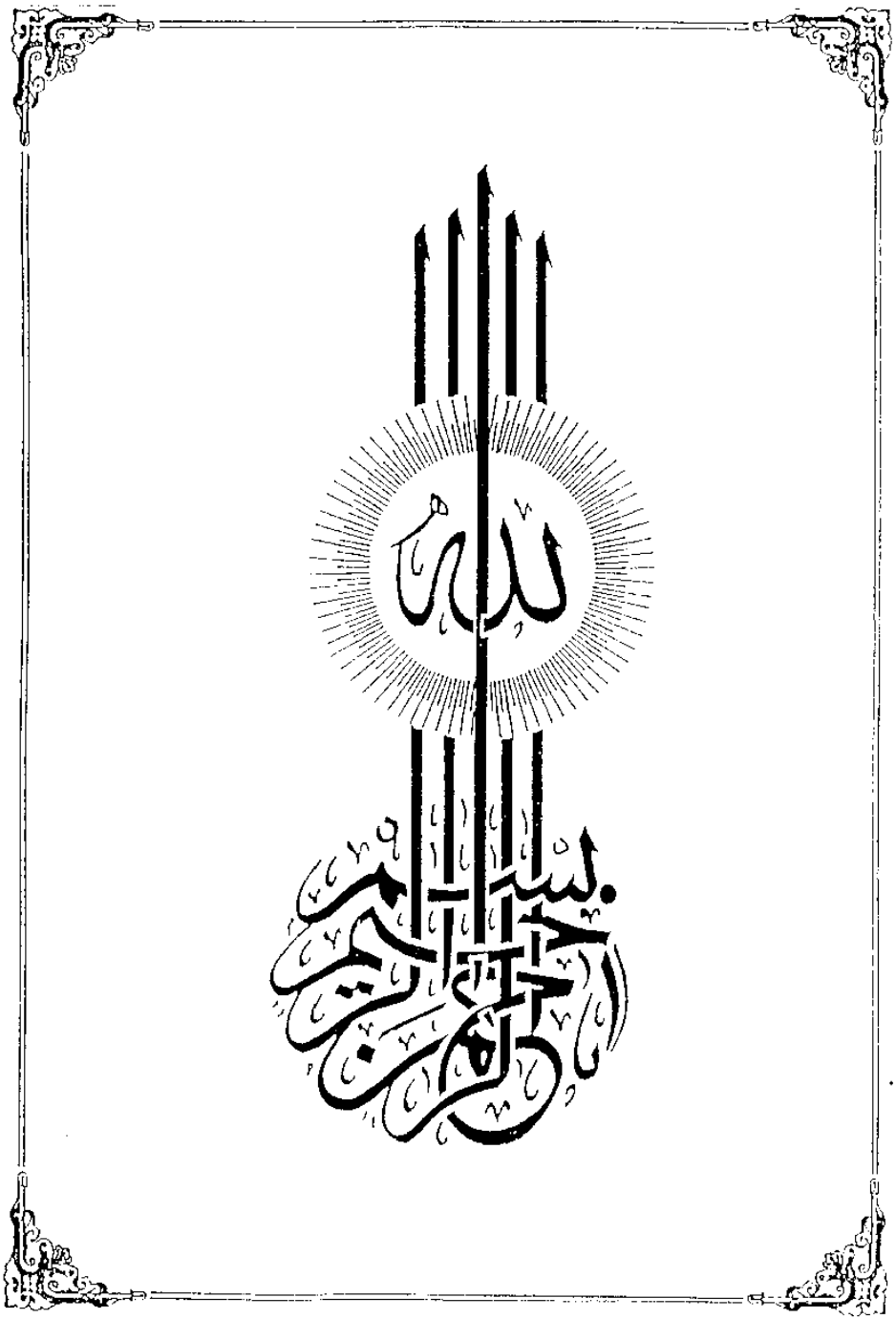
بسم الله الرحمن الرحيم

وقل رب زدني علما

صدق الله العظيم



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INTRODUCTION

INTRODUCITON

According to Mc-Kay et al. (1981) the term tumor marker means any identifiable change in a body component that is indicative of the presence of tumor. One of these tumor markers is steroid hormone receptors which is of importance in most gynecologic tumors.

Because sex steroid hormones control the growth and differentiation of female reproductive organs, their influence on tumor arising from tissues is not unexpected. (British medical, 1977; Kiang, 1981, Ehrlich and Young, 1981; Kohorn, 1981; Swenerton, 1982; Gambrell et al., 1983).

Steroids appear to enter the cell by passive diffusion (Peck et al., 1973) but are retained and probably concentrated in steroid responsive cells by specific receptors that bind the hormone firmly (Leake, 1981). Until recently, it was thought that these receptor were located in the cell cytoplasm and that they only translocated to the nucleus after binding with the hormone had induced a modification in the receptor structure (Leake, 1981). However recently, two groups of workers, using different techniques, produced new evidence that the normal location for the receptors may be in the nucleus or on the nuclear membrane (King & Green, 1984; Welshons et al., 1984). The presence of receptors in the cytoplasm is probably an artifact caused by the

homogenisation used in the cell fractionation process (Martin & Sheridan, 1982).

The presence of estrogen receptors (ER) in normal target tissues such as breast or uterine epithelium is generally accepted as a marker for estrogenic regulation of their growth and activity. Likewise, the presence of estrogenic receptors in malignant mammary tissue is believed to indicate the potential estrogenic regulation of the cancer. Although cytosolic estrogen receptors are used as guide to the selection of those patients with advanced disease who might benefit from endocrine manipulative therapy, their presence is associated with a response to endocrine therapy in only 50-60% of patients (Hawkins et al., 1980).

Also the presence of these estrogenic receptors in the leiomyoma in rich amount indicate that estrogen promotes the growth but does not initiate such growth and its role is supported by the tendency of these tumors to stabilize or regress after menopause, their frequency in nulliparas and their increase in size during pregnancy or with birth control pills (Samaha, 1986).

Martings et al. (1982) stated that it appears that estrogen receptors status has a prognostic value in cervical carcinoma as well as in breast carcinoma.

Although normal, premenopausal endometrial epithelial cells contain both estrogen and progesterone receptors

throughtout the menstrual cycle, it is clear that not all endometrial cancer cells are receptor positive. Whether this due to de-differentiation or to initial transromation of a "stem" cell is unclear. However, receptor positivity appears to decrease as histological grade increases. This observation is completed by intratumoral variation not only of receptor content but also of receptor status. Receptor status has some value as a prognostic index of survival and of disease-free interval but further study is required. Receptors status, seems to be exceptionally accurate in terms of selecting patients who will respond to endocrine therapy and those who will not. Prior induction of progesterone receptor with tamoxifen may be of further value in enhancing the effect of progesting therapy (Soutter and Leake, 1987).

The incidence of cytoplasmic estrogen receptor (CER) and cytoplasmic progesterone receptor (CPR) in benign tumors was similar to but some-what lower than that in normal tissues, with the difference being more segnificant with respect CPR status (Vihko et al., 1983; Will-Cooke et al., 1983 and Lanta, 1984).

Gronroos et al. (1984) found that the value of steroid receptor deteminations in selsecting the proper hormonal treatement in ovarian cancer is significantly reduced because of the high proportion of incorrect predictions.

AIM OF WORK

Aim of the work:

To review the sex steroid hormone receptors as regard of their nature, composition, mode of actions and importance as a prognostic value in cases of gynecologic tumors (breast, endometrium, cervix and ovary,.....).

TUMOR MARKERS

Tumor Markers

Definition:-

According to Mackay et al. (1981) the term tumor marker means any identifiable change in abody component that is indicative of the presence of cancer. Benjamini et al. (1981) stated that tumor cells are known to express cytoplasmic, cell surface, or secreted products that are sufficiently different in quantity or quality from products of normal cells to act as "tumor markers". Many of these are termed antigens, because they are identified by antisera raised in another species. Most tumor markers consist of excessive production of a normal product or production of material normally produced during development but present not at all or only in very low quantities in adults (a codevelopmental markers). Hakomori and kannagi (1983) stated that concer is associated with abnormalities in gene regulation expressed in multiple molecules at the cell surface membranes. Glycolipids are one of these molecules. they also explained that malignant transformation may be associated with blocked glycolipid synthesis and precursor accumulation, or neosynthesis of glycolipids unique to the tumor. Either mechanism induces an accumulation of a glycocipid characteristic of tumor cells but absent or present in small quantities in non transformed cells. These glycolipid tumor markers are hardly immunogenic to the host

and are shared with various types of tumors, they are therefore distinctive from classical "tumor associated antigen" and the term "tumor marker" is more appropriate. (Hakomori and Kannagi, 1983).

Barlow and Bhattacharya (1983) stated that elevated serum levels of galactosyl transferase in cancer patients suggests that abnormal antigens detected in cancer patients reflect altered glycoprotein mechanism.

The ideal tumor marker The ideal tumor marker should fulfill the following criteria: (according to Mackay et al. (1981) and Bates and Lango (1985).

(1) It should be relatively specific for cancer. Ideally, it should indicate not only the presence of cancer but its site of origin.

(2) It should not be present in healthy individuals or in those suffering from benign disease.

(3) It should be easily detected and measured.

(4) It should be detected in the earliest growth phase of the tumor allowing screenig of a symptomatic individuals.

(5) The amount of tumor marker should reflect the bulk of tumor present.

(6) It should decrease with successful treatment and increase with early recurrence.

(7) It should be inexpensive to detect.

Bates and Lango (1985) stated that no tumor marker described to date meets all of these criteria.

Classification of tumor markers According Mackay et al. (1983) tumor markers classified into

[1] Structural:- Microscopic (Cytology).

Submacroscopic (Colposcopy).

[2] Biochemical:

A- Non specific (present in a variety of tumor types)

- tumor derived: Hormones, enzymes, fetal proteins, placental proteins, nucleic acid derivatives.
- Host derived: Acute phase proteins, hydroxyproline.

B- Specific (Unique to a single tumor type)

- tumor antigens, antibodies and immune complexes.
- cell mediated reactions.
- blocking factors.

Structural: Cramer and Cutler (1979) pointed out that the first large scale marker to be employed was a morphological one and was based upon the detection of cytological changes in the abnormal Papanicolaou smear. The wide spread use of vaginal cytology since then has resulted in a marked decrease in the incidence of carcinoma of the cervix. Cytology, in turn directed attention to colposcopy which depend on grosser morphological changes-chiefly increased