A correlative study between breast lesions and ovarian pathology

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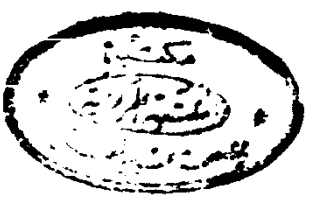

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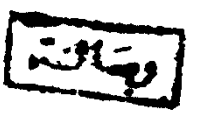

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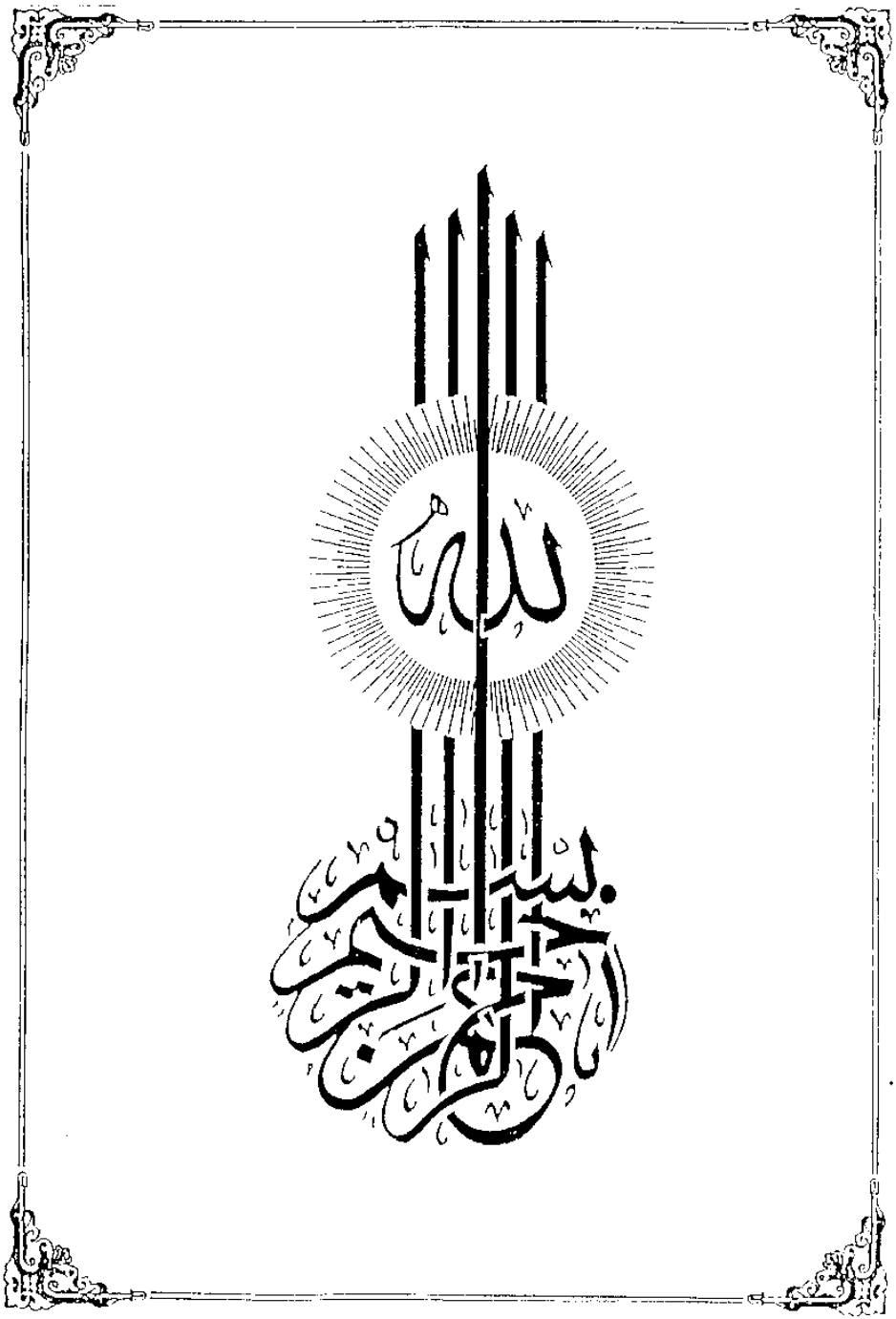

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INTRODUCTION

The relationship between hormones and neoplasia has been greatly clarified in the recent years (Bielschowsky and Horning, 1958 and Bonser and Jull, 1960).

Earlier workers had noted that ovariectomised mice seldom developed breast cancer, and in 1933 Lacassagne successfully produced mammary cancers in mice of both sexes by administering large doses of oestrogen. In man hormones are not usually an important factor in causing cancer (walter, 1974). However, there are some exceptions:

(a) granulosa-cell tumours of the ovary, which produce large amounts of oestrogen, lead to great endometrial hyperplasia which may occasionally proceed to carcinoma of the body of the uterus.

(b) men who have undergone artificial sex change and have taken large doses of oestrogen in order to produce breast enlargement, occasionally develop breast cancer (Symmers, 1968).

(c) men who receive large doses of oestrogen for treatment of prostatic carcinoma occasionally develop breast carcinoma.

Walter (1974) stated that while hormones play only a small role in the etiology of human cancer, they are perhaps of greater importance in maintaining the growth of some tumours. These are called hormone dependent tumours. Such neoplasms depend on specific hormones for their continued growth, and if deprived of them, undergo regression only to recur when the hormone is restored.

The breasts are known to be responsive target organs for oestrogen and progesterone. Hence any possible alterations in the breast epithelium after prolonged use of oral contraceptives, i.e. combination of these two hormones, must be taken into account (Erb, 1972). Several reports in the literature deal with the functional and clinical alterations in the human breast in women taking the contraceptive pills (Goldenberg et al, 1968; Gregg, 1966 and Schachner, 1966).

In female dogs contraceptives may induce breast adenomas.

The cancer-inducing capacity of oestrogen, above the physiological level, in rodents, is well known and already mentioned.

Metaplastic changes in the breast of monkeys treated with ethynerone have also been reported (Hertz, 1969).

Breast cancer manifests hormone dependence in less than half of the affected patients.

In premenopausal women with cancer breast oophorectomy removes the major source of oestrogens and progesterone. Hence it often produces a remission usually lasting about 6 months, but occasionally up to several years.

Bilateral adrenalectomy is sometimes performed at the same time to eliminate the other source of these hormones. In post menopausal women hypophysectomy is sometimes recommended.

Since most cases of breast cancer are hormone dependent from the start, much research has been undertaken to determine which patients are most likely to respond to hormone therapy.

This consists of assays of steroids in the urine. The results are inconclusive, and treatment is still a matter of trial and error (Walter, 1974). However, little if any investigation were carried out

to speculate ovarian changes that may be associated with and perhaps play a role in the pathogenesis of breast neoplasms (Sternberg and Gaskill, 1950; Novak and Mohler, 1953; Schneider and Bechtel, 1956 and Roddick and Green, 1958).

The aim of the present work is to correlate endometrial changes, vaginal cytology, and ovarian pathology with breastlesions, so as to elucidate an easier and rapid histopathological tool for earlier recognition and suspect of breast cancer. In addition these studies may spot light upon the pathogenesis and prognosis of these neoplasma.

Investigations in this work are carried out on 130 breast specimens, 129 endometrial biopsy specimens, 5 ovarian biopsies and 129 vaginal smears taken from in-patients in surgical department, Ein Shams University Hospital.

They are classified into the following groups:

1- Patients with inflammatory breast lesions.

2- Patients with hyperplastic breast lesions.

3- Patients with benign breast lesions.

4- Patients with breast cancer.

In all groups the following studies will be involved:

1- Histopathological examination of the breast lesions.

2- Endometrial biopsy taken by the suction curette.

3- Vaginal smear for cytological examination.

The last two items will indirectly reflect the ovarian changes. In the cancer group sections prepared from ovaries removed by oophorectomy will directly illustrate the ovarian pathology.

ANATOMY AND HISTOLOGY OF THE BREAST

The human breast is an accessory organ of the reproductive system. Structurally and embryologically, it appears to be a modified sweat gland.

The mammary glands lie directly over the pectoralis major from the second to the sixth rib anteriorly and from the sternum to the anterior axillary line. They have the aspect of of a hemisphere in the middle of which there is a prominent papilla, the nipple, surrounded by an area of pigmented skin called the areola. With advancing age, the breast becomes some what flattened, pendulous, and less firm. The gland is incased in a layer of fat except in the region of the nipple and areola. Posterioly the fatty tissue forms a cushion that permits movement of the gland over the pectoralis muscle. Anteriorly its convex surface is irregular due to the presence of salient fibrous crests. These crests form the deep attachment of fibrous septa (so called cooper's ligaments). Cooper's ligaments run between the superficial and deep fascia; the superficial fascia is attached to the skin. The upper outer quadrant is thicker than the remainder of the breast. It contains the greater bulk of the mammary parenchyma which may account for

the fact that both benign and malignant tumours are more frequent in that site (Haagensen, 1971). Sixty percent of breast carcinoma arise in that quadrant (Marshall and Higginbotham's stastistics, 1965). Supernumerary breasts with or without corresponding nipples are observed in men and women. They are frequently found below and medial to the normal breast, overlying the pectoralis major muscle at the anterior axillary line, or in the hollow of the axilla.

The mammary gland is made up of twelve to twenty glandular lobes; each one with a ramified duct. These ducts are irregular and tortuous and travel in the direction of the nipple. Close to the nipple they dilate to form the ampullae and then devide into minute ducts which finally end in small opening in the nipple. The ducts and acini have two fibrous coverings:

1- An inner periductal or periacinar, layer which is hormone dependent and increases in states of normal breast activity. It contains few lymphocytes and proliferates in cases of benign fibroadenomas.

2- An outer layer, the perilobular connective tissue,

which does not differ from the ordinary fibrous tissue found else where in the body. It is not controlled by hormones and does not take an active part in any of the pathologic changes which spontaneously affect the true breast structures. The cells of the acini are cuboidal in shape, whereas those of the lactiferous ducts are columnar. The epithelial elements of both acini and ducts are enveloped by a delicate, well defined argyrophilic collagen sheath or basement membrane. A contineous layer of myoepithelial cells lie between the lining epithelium and the basement membrane best seen in the smaller ducts and thins out as it approaches the acini and large collecting ducts. The myoepithelial cells are elongated contractile cells closely resembling smooth muscle cells. Though they are epithelial in origin. They are arranged spirally around the ducts and they provide a muscular mechanism for ejecting milk from acini and ducts (Richardson, 1945 and Linzell, 1952). This mechanism is controlled by hormonal or metabolic factors. No innervation of these cells could be demonstrated by careful histologic studies. Outside the basement membrane, lies the elastica which surrounds the ducts and abruptly terminates where the acini begin. Occasionally a thin

layer of elastica surrounds some acini and lobules. The medium and large sized ducts are surrounded by a layer of unstriated muscle fibres.

The mamary gland varies instructure with age and during activity (pregnancy and lactation). Cheatle and Culter (1931) and Cutler (1961) described the histological appearance of the breast at the various stages of life from birth till menopause.

Morphologic appearances of the breast at birth. The development of the breast is not always complete at the end of 9 months of fetal life. The appearance of breasts varies. But, common to all breasts at birth, the elastica has formed around all ducts. In some breasts only few acini can be seen, and ducts form the chief part of the gland. In some instances large, irregular shaped columns of epithelium may be seen dipping into the subcutaneous tissue to form future ducts and acini. In other instances the pericanalicular and periacinar connective tissue is enormous in amount, and lymphocytes can be seen scattered amongst its fibers. Also, epithelial elements may be under going a desquamative hyperplasia. When the two latter conditions are combined in one breast, the morphologic appearance of a breast at

birth exactly resembles the condition now commonly termed "chronic mastitis" of later life. Very rarely, a type of desquamative epithelial hyperplasia may be seen which we describe as being the cystic type.

Dietrich's (1927) studies have shown that in newborn infants the glands are hypertrophied and composed of a double layer of epithelium surrounded by pericanalicular and periacinar tissue of the breast. Round cell infiltration is a common features, and its presence is more indicative of a physiologic process than a pathologic state. In other breasts the epithelial proliferation may be so great as to resemble a lactating breast. In its most pronounced state the activity of the epithelium may be so marked and the space in which they are confined so large that the observer, without a knowledge of the history, would feel compelled to consider the possibility of malignant change.

Between birth and puberty. The breastn is in a state of quiescence. The lobules have formed, there is very little pericanalicular and periacinar tissue and only few acini. The epithelium lining the ducts and the acini is inactive and is not undergoing any form of

hyperplasia.

At puberty: The mammary gland becomes large in size due to deposition of fat and growth of the fibrous tissue stroma. New ducts and lobules of acini are formed and there is hyperplasia of the periacinar and pericanalicular fibrous connective tissue, among which lymphocytes may be present. There may be desquamative epithelial hyperplasia in ducts and acini.

Histologic structure of a resting breast: The breast of a sexually mature nonpregnant female is termed a resting breast. In the resting condition the mammary gland contains very little glandular tissue and a relatively large amount of areolar and adipose tissues. Each gland is formed of a number of lobes which are drained by a corresponding number of lactiferous ducts, opening on the summit of the nipple. The ducts are swollen under the areola, where they form the latiferous sinuses. The lobes are divided into further lobules. The intralobular connective tissue is loose, being formed of cells, a few fibers and practically no fat. This is meant to give place for the glandular tissue during development. On the contrary, the interlobular connective tissue is more dense,