

CLINICAL SIGNIFICANCE OF THE cAMP LEVEL IN BENIGN AND MALIGNANT BREAST DISEASES



Thesis

Submitted for Partial Fulfillment of
The M.D. Degree in *General Surgery*

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To...

My Father and Mother,

My Wife,

My Sons Mohamed and Mahmoud

My Family

Ahmed

Acknowledgement

I am honored to have Prof. Abdel Meguid El-Shinnawy, Professor of Surgery, Faculty of Medicine, Ain Shams University, to supervise this work and I am indebted to him for his valuable advices and continous guidance without which this thesis would have not been delivered in this form.

I would also wish to express my profound thanks for Professor Aly Khalifa, Professor of Biochemistry, Faculty of Medicine, Ain Shams University, for the help he provided me and for his time, effort and advice during the production of this thesis.

Also I wish to express my deep thanks to Professor Salwa Hadad, Dr. Ahmed Abdel Aziz, Dr. Sanaa Eissa for their cooperation and fruitful help and continuous guidance.

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Introduction

INTRODUCTION

Breast cancer is the most common malignancy affecting females in most parts of the world including Egypt. Statistical reports from The national Cancer Institute in Cairo show that breast cancer accounts for 34.8% of the total malignant diseases among Egyptian females (*Ibrahim and Aref, 1983*).

Recently, our understanding of the biologic behaviour of breast cancer has changed dramatically. It is now believed that breast cancer is a systemic disease that disseminates very early to the systemic circulation (*Coombes et al., 1983*).

The only hope for better prognosis in breast cancer patients, seemingly, is in early detection (*Wynngarden and Smith, 1988*).

Not surprisingly, many trials have been constructed evaluating the value of breast cancer screening, the results of which are so far encouraging (*Johnson and Taylor, 1992*).

Cyclic adenosine monophosphate (c-AMP) is a second messenger in many hormonal actions and many studies have

been explored its possible role in carcinogenesis, and it has been shown to be elevated in a progressive fashion from normal breast tissue to fibrosis, fibroadenosis, ductular hyperplasia and finally to carcinoma. Benign breast lesions with significantly higher c-AMP levels, although still lower than those of cancer, must be considered at higher risk for eventual malignant change (*Minton et al., 1985*).

The aim of this study is to evaluate c-AMP as a significant biochemical marker in benign and malignant breast diseases.

Review of Literature

Developmental Anatomy of the Breast

During the fifth week of human fetal development, the ectodermal primitive milk streak, or galactic band develops from axilla to groin on the embryonic trunk. In the region of the thorax, the band develops to form a mammary ridge, whereas the remaining galactic band regresses. Incomplete regression or dispersion of the primitive galactic band leads to accessory mammary tissues, found in 2% to 6% of adult women. The breast develops on upper part of the milk ridge. Solid ingrowth from the surface ectoderm occurs to form the duct system and secretory part of the gland while the stroma is derived from the mesenchyme (*Michael, 1987*).

The evolution of the breast from childhood to maturity has been divided into five phases. It occurs under the effect of estrogen and progesterone which together produce full ductular-lobular-alveolar development of mammary tissues. In phase I (age : Puberty), there is elevation of the nipple with no palpable glandular tissue or alveolar pigmentation. In phase II (age :11.1±1.1); glandular tissue exists in the subareolar region and

both nipple and breast project as a single mound from the chest wall. In phase III (age : 12.1 ± 1.09 years), there is increase in the amount of readily palpable glandular tissue with enlargement of the breast and increased diameter and pigmentation of the areola. The contour of the breast and nipple remains in a single plane. Again in phase IV (age : 13.1 ± 1.15 years), enlargement of the areola and increased areolar pigmentation occurs. The nipple and areola form a secondary mound above the level of the breast.

Finally, adolescent development of a smooth contour with no projection of the nipple and areola occurs in phase V (*Harris, 1988*).

The adult breast lies between the second and sixth ribs in the vertical axis, and between the sternal edge and mid axillary line in the horizontal axis. Breast tissue also projects into axilla as the axillary tail of Spence. The breast is composed of acini which make up lobules, aggregations of which form the lobes of the gland. The lobes are arranged in a radiating fashion like the spokes of a wheel and converge on the nipple, where each lobe is drained by aduct. Ten to fifteen collecting ducts open onto the nipple, each duct draining a segmental system of smaller ducts

and lobules. The breast is anchored to the overlying skin and to the underlying pectoral fascia by bands of connective tissue called Cooper Ligaments (*Decker, 1986*).

The principal blood supply to the breast is derived from the internal mammary and lateral thoracic arteries. Approximately 60% of the breast, mainly the medial and central parts, is supplied by the anterior perforating branches of the internal mammary artery. About 30% of the breast, mainly the upper outer quadrant, is supplied by the lateral thoracic artery.

The breast drains mainly to the axillary nodes receiving about 75 percent of lymph draining the breast tissue.

In the immature breast, the ducts and alveoli are lined by a two layer epithelium consisting of a basal cuboidal layer and a flattened surface layer. In the presence of estrogens at puberty and subsequently, this epithelium proliferates, becoming multilayered. Three alveolar cell types have been observed : superficial (luminal). A-cells, basal B-cells (Chief cells), and myoepithelial cells (*Harris, 1988*).

During pregnancy, marked ductular, lobular, and alveolar growth occurs as a result of the influence of luteal and placental sex steroids, placental lactogen, prolactin, and chorionic gonadotropin.

In the first 3 to 4 weeks of pregnancy, marked ductular sprouting occurs with some branching, and lobule formation occurs under estrogenic influence. At 5 to 8 weeks, breast enlargement is marked, with dilatation of the superficial veins, heaviness, and increasing pigmentation of the nipple-areolar complex. In the second trimester, lobule formation exceeds ductular sprouting under progestogenic influence. The alveoli contain colostrum but no fat, which is secreted under the influence of prolactin. From the second half of pregnancy onward, increasing breast size results from dilatation of the alveoli with colostrum, as well as hypertrophy of myoepithelial cells, connective tissue and fat (*Richard, 1988*).

Following parturition, an immediate withdrawal of placental lactogen and sex-steroid hormones occurs. During pregnancy, these hormones antagonize the effect of prolactin on mammary epithelium. Prolactin, in the presence of growth

hormone, insulin, and cortisol converts the mammary epithelial cells from a prescretory to a secretory state. During the first four or five days after birth, the breasts enlarge owing to the accumulation of secretions in the alveoli and ducts. Following colostrum secretion, transitional milk and then mature milk are elaborated (*Richard, 1988*).

Involucional changes of the breast are usually obvious by the age of 35. The changes include disappearance of lobular epithelium and replacement of lobular connective tissue by more fibrous tissue usually found in the inter lobular region (*Kevin, 1992*).