New trends in the management of early breast cancer

A protocol of an essay

Submitted for partial Fulfillment of
MASTER DEGREE IN GENERAL SURGERY

BY

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ABSTRACT

Background and objectives: The magnitude of the breast cancer problem emphasizes the need to determine the best possible predictors of prognosis so that appropriate therapy can be selected on an individual basis for women suffering from this common and dreadful disease. Axillary lymph node dissection is an effective staging procedure and is essential for local control of disease in axilla. Variations in axillary anatomy have not been described in most texts of operative surgery or anatomy. So, come the importance to determine the potentially involved groups of axillary lymph node in patients with breast carcinoma. Hence, the aim of this work was highlight on the pattern of axillary node metastasis in-patients with operable breast cancer and to detect any variations in the sites of lymph node groups to be involved.

Methods: Fifty female patients with operable breast cancer were treated surgically by modified radical mastectomy, (46 patients) radical mastectomy (Three patients) or breast conserving surgery (one patient), in the National Cancer Institute, Cairo University, in the period from December 1998 to April 2000, as a prospective non-randomized study. The brachial nodes were defined in this work as the pad of fat containing lymph nodes anterior and above the cords of brachial plexus, behind the insertion of pectoralis minor muscle and medial to coracobarchialis muscle. This pad of fat, which was taken separately, was examined carefully to detect the presence of any lymph nodes and these lymph nodes were examined microscopically and any positive lymph nodes were calculated.

Results: Thirty-seven patients (74%) were premenopausal (below age of 50 years and younger) and 13 patients were postmenopausal (26%) (above age of 50 years). Invasive duct carcinoma was the commonest type 84%. Patients with stage II constituted 84%, and those of stage III were 16%. Among 50 patients, 41 patients showed pathological involvement of lymph nodes (82%) and nine patients (18%) had no lymph nodes deposits. The number of lymph nodes that were examined in the 50 patients ranged from 10 to 30 lymph nodes with a median of 18.5 lymph nodes. The brachial nodes were detected in 22 patients of the 50 patients (44%). Their number ranged from one to four lymph nodes. However, only two patients of 50 patients of this study (4%) proved to have positive brachial lymph nodes. It worthnothing that in these two patients with positive brachial lymph nodes, all the three levels of axillary nodes had also positive nodes. In the two previous patients the tumor was T2 (4 cm in each) and invasive duct carcinoma, both patients were premenopausal. The incidence of positive lymph nodes in 41 patients with positive nodes was; in level 1 only 56%, level I&II it was 19.5%, and in the three levels was 22%. One patient showed involvement of level III alone with no lymph node metastasis in level I to II (skip metastasis). Moreover, two patients (2/41 patients) represented (4.9%) had positive brachial lymph nodes with positive three levels of axillary nodes. Capsular invasion was evident in 22/41 patients with positive axillary lymph nodes. This study showed that whatever the tumor site in the breast, the axillary lymph nodes were commonly affected especially, level I. It was also observed that; as the tumor size increased more lymph node levels were involved.

Conclusions: Complete axillary lymph node dissection is advisable in all patients with invasive breast cancer for proper staging and therapeutic purposes As, Level III dissection is probably superior to radiotherapy in preventing axillary relapse, when it occurs a miserable condition that is difficult to treat due to involvement of axillary vessels and cords of brachial plexus. Clearance of the brachial nodes (which lie anterior and above cords of brachial plexus) may decrease incidence of axillary recurrence with no morbidity; however, further work is required to determine the exact incidence of metastasis in these nodes.

Key Words: breast cancer, axilla, axillary lymph node metastasis, brachial lymph nodes.

Acknowledgement

First of all; All gratitude is to ***god*** who guided and aided me to bring to light this work.

I would like to express my sincere thanks and deepest gratitude to ***Prof. Dr. Raafat Gohar***, Professor of general and plastic surgery, Cairo University, for giving me the privilege to work under his supervision and for giving me his valuable advices.

Many thanks to ***Prof. Dr. Moustafa Ahmed Abu-Elsoud***, Professor of general and plastic surgery, Cairo University, for his great support and encouragement throughout this work.

Words are not enough to express my great thanks and deep appreciation to ***Prof. Dr. Ashraf El-Sebaei,*** Professor of general and plastic surgery, Cairo University, for his comments, ideas, constructive criticism and support throughout this essay.

I would also thank ***all my family*** for their support and encouragement throughout this work.

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List of abbreviations

ACOSOG = The American College of Surgeons Oncology Group.
ADH = Atypical ductal hyperplasia.
ALH = Atypical lobular hyperplasia.
ALMANAC = The Axillary Lymphatic Mapping Against Nodal Axillary Clearance.
ALND = Axillary lymph node dissection.
ALNs = Axillary lymph nodes.
ANS = Axillary lymph node sampling.
Apo A1= Apoprotein A1.
A.T.M. = Ataxia telangiectasia.
BCA = Breast cancer antigen.
BCS = Breast conservative surgery.
BCT = Breast conservative therapy.
BPM = Prophylactic mastectomy.
BRCA-1 = Breast cancer antigen 1.
BRCA-2 = breast cancer antigen 2.
CEA = Carcino-embryonic antigen.
CMF = Cyclophosphamide, Methotrexate and Fluorouracil.
CV. flap = Central core flap.
DCIS = Ductal carcinoma insitu.
DIEP = Deep inferior epigastric perforator flap.
EBCTCG = The early breast cancer Trialists Collaborative Group.
EIC = Extensive intra-ductal component.
EORTC = The European Organization for Research and Treatment of Cancer.
E.R. = Estrogen receptor.
ER –ve = Estrogen receptor negative.
ER +ve = Estrogen receptor positive.
FDA = Food and Drug Administration.
Fig. = figure.
FNAC = Fine needle aspiration cytology.
F-ve = False negative.

F+ve = False positive.
FNR = False negative rate.
FPR = False positive rate.
HDLc= High density lipoprotein C.
IBCSG = The International Breast Cancer Study Group.
I.H.C. = Immune-histochemistery.
IMNs = Intra-mammary nodes.
LCIS = Lobular carcinoma insitu.
LR = Local recurrence.
M.D.R. = Multiple drug resistance.
MRI = Magnetic resonance imaging.
MRM = Modified radical mastectomy.
MSKCC = The Memorial Sloan- Kettering Cancer Center.
NAC = Nipple-areola complex.
NPI = Nottingham prognostic index.
NSABP = National Surgical Adjuvant Breast and Bowel Project.
NSN = Non-sentinel lymph node.
PDMS = poly-di-methyl-siloxane.
PET = Positron emission tomography.
PN = Pathological lymph nodes.
PS2 = protein S2.
ROM = Range of motion.
RT = Radiotherapy.
SLN = Sentinel lymph node.
SLNB = Sentinel lymph node biopsy.
SSM = Skin-sparing mastectomy.
T.g.= Triglyceride.
Tis = Carcinoma insitu.
TM = Total mastectomy.
T.N.M. = Tumor size. Lymph nodes. Metastases.
TRAM = Transverse rectus abdominis myocutaneous pedicle flap.
USA = United State of America.
VNPI = Van Nuys prognostic index.
W.H.O. = World Health Organization.

Introduction

Introduction

Breast carcinoma is a malignant epithelial tissue tumor of the breast. It is estimated that the world burden of the breast cancer is some one million women newly diagnosed each year. A women has a 1 in 8 chance of developing breast cancer at some point in her life, the incidence has been increasing over the last several years by approximately 1% each year. Cancer of the male breast is uncommon comprising less than 1% of all breast cancer. Klinefelter's syndrome and elevated estrogen levels have been associated with male breast cancer ***(Bruce Jarrell. et. al, 2003).***

Clinically breast cancer is presented by either breast lumps, breast pain, metastatic disease to a distant organ or to the axillary lymph nodesor breast cancer may be asymptomatic. There are 2 clinical classifications for breast cancer either, Manchester which classifies breast cancer into 4 stages from I to IV or T.N.M. classification which classifies breast cancer according to tumor size {T}, presence or absence of lymph nodes {N} and presence or absence of metastasis {M} ***(Martin. et. al, 2002).***

Investigations for breast cancer include mammography, ultrasound, biopsy {either fine needle aspiration, core needle biopsy, excisional biopsy or needle guided biopsy for non-palpable mammographic abnormalities}, CT and recently MRI is used for diagnosis of breast cancer ***(Leris. et. al, 2004).***

Treatment of breast cancer is mainly surgical, conservative surgery is the treatment of choice for malignant tumors at least up to stage II. Conservative surgery includes wide local excision, segmental excision or quadrantectomy, both wide local excision and segmentectomy would normally be followed by radiotherapy. Randomized controlled clinical trials have shown that in tumors up to 4 cms. In size, treatment by mastectomy or breast conservation results in no significant difference in overall survival. Patients undergoing conservative surgery have greater freedom of dress and better body image than women who have had mastectomy, local recurrence rate are similar with a non significant relative reduction in favor of mastectomy ***(Alfred Cuschieri. et. al, 2003).***

Quadrantectomy if not followed by reconstruction {eg. a latissimus dorsi mini flap} produces less good cosmetic results than wide local excision or segmental excision. A central tumor is not a contra-indicated to conservative surgery although it may necessitate removal of the nipple and areola which may compromise cosmesis **(*Alfred Cushierei. et. al. 2003).***

Radiotherapy given after surgery reduces the risk of isolated local recurrence by approximately 2/3, thus radiotherapy is of potential benefit to all patients undergoing breast conservative surgery and should only be omitted if the clinician feels-after discussion with the patient-that the morbidity of radiotherapy does not justify the excess recurrence risk for that patient ***(costa. et. al, 2004).***

Adjuvant systemic therapy includes endocrine therapy as tamoxifen which is an antiestrogen blocking estrogen receptor alpha and is the most widely used adjuvant systemic therapy for most postmenopausal women, ovarian ablation is of benefit to premenopausal women. Cytotoxic chemotherapy, regimen was a combination of cyclophosphamide, methotrexate and 5-fluorouracil {CMF}. Recently, 5 fluorouracil, adriamycin, and cyclophosphamide {FAC} are used, the current studies results stressed the value of primary chemotherapy to increase conservative surgery and as a predictor of outcome ***(Falo. et. al, 2005).***

Neoadjuvant chemotherapy involves giving chemotherapy before surgery to patients with non-metastatic primary breast cancer which is potentially operable ***(Calitchi. et. al, 2001).***

The performance of breast augmentation is increasing at an estimated rate of 5% to 13% per year, making it one of the most commonly performed cosmetic surgical procedures in women. First attempted in 1895 using a patient's own lipoma, breast augmentation has since been undertaken with a variety of solid substances including paraffin, ivory, glass balls, ground rubber, ox cartilage, wool, polyester, silastic rubber, and injections of beeswax, Vaseline, silicone, shellac, glazier's putty and epoxy. At present, augmentation is performed with sub-mammary or sub-pectoral implants filled with saline or silicone, although women who have had free silicone injections in the breast are still seen in clinical practice ***(Richard. et. al, 2008).***

Aim of study

The study aims to present the new trends in the management of early breast cancer as conservative surgery with radiotherapy and chemotherapy, followed by immediate or delayed breast reconstruction.

Chapter (1)

Anatomy of breast

Anatomy of the breast

Development:

Breast develops as an invagination of chest wall ectoderm, which forms a series of branching ducts. Shortly before birth this site of invagination everts to form the nipple. The epithelial lining of the ducts and acini of the mammary glands develops from the ectoderm and the supporting tissue is derived from the mesenchyme. On each side of the ventral surface of young embryos, a thickened band of ectoderm develops (mammary ridge). It extends obliquely from the axilla to the inguinal region. The whole of the ridge atrophies, except a small portion in each pectoral region from which the breast arises ***(McMinn. 2003).***

Gross anatomy

Form and size:

The breast is located within the superficial fascia of the anterior thoracic wall. It consists of 15 to 20 lobes of glandular tissue of the tubuloalveolar type. Fibrous connective tissue forms a frame work that supports the lobes, and adipose tissue fills the space between the lobes. Subcutaneous connective tissue surrounds the glands and extents as septa between the lobes and lobules, providing support for the glandular elements, but it dose not form a distinctive capsule around the components of the breast. The deep layer of the superficial fascia which lies on the posterior "deep" surface of the breast rests on the pectoral "deep" fascia of the thoracic wall. A distinct space, the retro mammary bursa, can be identified surgically on the posterior aspect of the breast between

The deep layer of the superficial fascia and the deep investing fascia of the pectoralis major and contiguous muscles of the thoracic wall (Fig.1). The retro mammary bursa contributes to the mobility of the breast on the thoracic wall. Fibrous thickening of the connective tissue interdigitate between the parenchymal tissue of the breast, extending from the deep layer of the superficial fascia and attached to the dermis of the skin. These suspensory structures called Cooper's ligaments, insert perpendicular to the delicate superficial fascia of the dermis, or corium, permitting remarkable mobility of the breast while providing support ***(Kirby et. al, 1998).***

At maturity, the glandular portion of the breast has a unique and distinctive protuberant conical form. The base of the cone is roughly circular, measuring 10 to 12 cm. in diameter and 5 to 7 cm. in thickness. Commonly, breast tissue extends into the axilla called the axillary tail of Spence. There is tremendous variation in the size of the breast ***(Kirby et. al, 1998).***

A typical non lactating breast weighs between 150 to 225 gm. Whereas the lactating breast may exceed 500 gm. The breast of nulliparous female has a typical hemispheric configuration with a distinct flatting above the nipple. The multiparaous breast, which has experienced the hormonal stimulation associated with pregnancy and lactation, is usually larger and more pendulous. As has been noted during pregnancy and lactation the breast increases dramatically in size and becomes more pendulous. With advanced age the breast usually decreases in volume, becomes somewhat flattened and pendulous, and is fewer firms ***(Kirby et. al, 1998).***