

New Trends In Management Of Early Breast Cancer

Essay

Submitted for partial fulfilment of M.sc. degree

BY

Reda Attia Abdelsalam

M.B.B.CH

Faculty of medicine- Al Azhar University

For partial fulfillment of master degree in general surgery

Under Supervision Of

Prof. Dr/ Aser Mostafa Al Afify

Professor of general surgery

Faculty of Medicine

Ain Shams University

Prof. Dr/Wael Abd Alazeem Jumuah

Assistant professor of general surgery

Faculty Of Medicine

Ain Shams University

Dr/Mohamed Aboul Naga

Lecturer of general surgery

Faculty Of Medicine

Ain Shams University

Faculty of Medicine

Ain Shams university

2017



فَالُوا سُبْحَانَكَ

لَا عِلْمَ لَنَا

إِلَّا مَا عَلَّمْنَا

إِنَّكَ أَنْتَ

الْعَلِيمُ الْحَكِيمُ



صِرَاقَ اللَّهِ الْعَظِيمِ

سُورَةُ الْبَقَرَةِ الْآيَةُ (32)



Acknowledgement

First and foremost, thanks to **"ALLAH"** for granting me the power accomplish this work;

I would like to express my endless gratitude and appreciation to **Prof. Dr. Aser mostafa Al Afify**, Professor of general surgery, Faculty of Medicine Ain Shams University for giving me the honour of working under his supervision and providing me with a lot of encouragement and support.

My deepest gratitude and appreciation are to **Dr. Wael Abd Alazeem Jumuah**, Assistant professor of general surgery, Faculty Of Medicine ,Ain Shams University for his acceptance to supervise my work for his continuous support, his valuable advice and encouragement.

My deepest gratitude and appreciation are to **Mohamed Aboul Naga**, Lecturer of general surgery, Faculty Of Medicine, Ain Shams University for his acceptance to supervise my work for his continuous support, his valuable advice and encouragement.

Reda Attla Abdelsalam



CONTENTS

| Subject | Page No. |
|---|-----------------|
| Contents | I |
| List of Tables..... | ii |
| List of Figures | iii |
| List of Abbreviations..... | iv |
| Introduction | 1 |
| Aim of the Work | 4 |
| Anatomy of the breast | 5 |
| Pathology..... | 23 |
| Diagnosis..... | 44 |
| Treatment of early breast cancer | 70 |
| Summary and Conclusion..... | 122 |
| References | 126 |
| المختص العربي..... | 1 |

LIST OF TABLES

| Table No. | Title | Page No. |
|------------------|---|-----------------|
| Table (1): | Stage grouping | 37 |
| Table (2): | Prognostic factors in node negative breast cancer: | 42 |
| Table (3): | Approximate Survival (%) of Patients with Breast Cancer by TNM Stage: | 43 |
| Table (4): | Threshold for treatment modalities according to the 2009 St. Gallen Consensus Conference..... | 111 |
| Table (5): | Important drug classes divided by known CYP2D6 inhibitory activity | 115 |
| Table (6): | Selected current adjuvant chemotherapy regimens | 117 |

LIST OF FIGURES

| <i>Figure No.</i> | <i>Title</i> | <i>Page No.</i> |
|-------------------|---|-----------------|
| Fig. (1): | The adult female breast. The upper and medial portions of the breast rest on the pectoralis major muscle, and the inferolateral portion rests on the serratus anterior | 7 |
| Fig. (2): | The mature resting lobular unit (Iglehart and Smith 2008)..... | 9 |
| Fig. (3): | Lymphatic drainage of the breast | 15 |
| Fig. (4): | Lymphatic drainage of the breast | 17 |
| Fig. (5): | A segment of the chest wall illustrating the relationship of structures to the ribs..... | 18 |
| Fig. (6): | Walls and contents of axilla | 21 |
| Fig. (7): | Inspection of the breast (a) From the front and (b) With arms raised | 48 |
| Fig. (8): | Palpation of the breast, (c) Palpation of the breast with the patient supine and (d) Palpation of the axilla..... | 49 |
| Fig. (9): | A 58-year-old asymptomatic woman undergoing yearly screening mammography. A, A spiculated mass is seen in the medial left breast on the CC view, isodense to breast parenchyma. On biopsy, this proved to be an invasive ductal carcinoma. B, In retrospect, the mass is evident on the study 2 years before, but is difficult to differentiate from glandular tissue. | 51 |
| Fig. (10): | Ultrasound-guided biopsy. The needle can be inserted into the lesion under ultrasound guidance | 54 |
| Fig. (11): | Sentinel node biopsy | 66 |
| Fig. (12): | Lumpectomy | 76 |
| Fig. (13): | Quadrantectomy | 77 |
| Fig. (14): | Therapeutic mastoplasty technique. (a) Preoperative lateral view showing location and size of tumor in lower outer pole of right breast (b) preoperative Wise pattern markings (c) postoperative results at 3 years. | 79 |
| Fig. (15): | Thoraco-epigastric flap technique. (a) Preoperative view the tumor is located above the left infra-mammary fold (b) intraoperative view showing markings for the thoraco-epigastric flap (c) postoperative view at 1 year | 80 |

LIST OF ABBREVIATIONS

| | |
|----------------|--|
| THR | : Total Hip Replacement |
| WHR | : waist-hip ratio |
| DCIS | : ductal carcinoma in situ |
| LCIS | : lobular carcinoma in situ |
| Her | : Human epidermal growth factor receptor |
| ER | : estrogen receptor |
| PR | : progesteron receptor |
| TNBC | : Triple-negative breast cancer |
| FISH | : fluorescence in situ hybridization |
| EIC | : extensive intraductal component |
| IBTR | : ipsilateral Bdeast Tumer Recurance) |
| MBI | : Molecular breast imaging |
| FNAC | : fine needle aspiraton cytology |
| CNB | : core needle biopsy |
| SLN | : Sentinel lymph node |
| ACBS | : American College of Breast Surgeons |
| H&E | : hematoxylin and eosin stain and |
| IHC | : immune histo chemistry (IHC) |
| ASCO | : American Society of Clinical Oncology |
| CEA | : carcinoembryonic antigen |
| CECs | : Circulating endothelial cells |
| EPCs | : endothelial precursor cells |
| CSCs | : cancer stem-like cells |

| | |
|---------------|---|
| TAAs | : tumor-associated antigens |
| RM | : Radical mastectomy |
| MRM | : Modified Radical Mastectomy |
| SSM | : Skin sparing mastectomy |
| NSM | : Nipple sparing mastectomy |
| BCS | : Breast conserving surgery |
| SLE | : systemic lupus erythromatosis |
| WLE | : wide local excision |
| LR | : local recurrence |
| IOMA | : intraoperative margin assessment |
| CTP | : cytologic touch preparation |
| SM | : , shaved margin |
| IOUS | : intraoperative ultrasound |
| PET | : Positron Emission Tomography |
| ROLL | : Radio-guided Occult Lesion Localization |
| NIRF | : Infrared Fluorescence |
| NAC | : nipple-areolar complex |
| RFA | : Radiofrequency Ablation |
| HIFU | : High-intensity focused ultrasound |
| ILA | : Interstitial Laser ablation |
| WBRT | : Whole breast radiotherapy |
| PBI | : partial breast irradiation |
| PMRT | : Postmastectomy radiotherapy |
| GnRHAs | : Gonadotropin-releasing hormone analogs |
| G-CSF | : granulocyte colony-stimulating factor |

Introduction

Breast cancer is the most common female cancer. World wide more than a million women are diagnosed every year. In the last ten years, female breast cancer incidence rate has increased by 13%, however, the mortality rate is declining (*keshtgar et al., 2009*)

Diagnosis of breast cancer can be carried out by triple assessment, which include clinical evaluation, breast imaging and tissue diagnosis (cytological or histological). Full-field digital mammography has allowed more confident identification of small clusters and microcalcifications. Digital equipment provides a major advantage in stereotactic procedures for impalpable lesions including guide wire placement, core biopsy and vacuum assisted excision where small lesions can be completely removed percutaneously using mammotome (*Gotzsche et al., 2009*)

Sonography is more sensitive than mammography in evaluating breast masses in young patients (*Houssami et al., 2003*).

The role of magnetic resonance imaging in the preoperative setting is still controversial. It is recognized as the most sensitive modality in identification and local staging of breast cancer (*Sardanelli et al., 2010*).

MRI has a higher negative predictive value(97% for a lesion of 2mm or More)for measuring the distance between nipple areolar complex and the lesion itself which is useful for planning nipple sparing mastectomy (*Peters et al., 2011*).

Sentinel lymph node biopsy has been generally adopted as an alternative procedure to axillary lymph node dissection in node staging (*De Boer et al., 2009*).

The routine use of preoperative axillary US and biopsy of abnormal nodes help in identifying high-risk patients and thus aids in planning treatment(*Roy et al.,2014*)

Skin sparing mastectomy followed by immediate breast reconstruction is used for prophylaxis for high-risk patients. It is also a surgical option for patients with large in situ lesions not accessible to breast conservation or to invasive breast cancer associated with extensive in situ disease (*Chunng and Sacchini, 2008*).

Radiofrequency ablation of small invasive breast cancer seems to be a feasible treatment option. Histopathological examination results in complete cell death of target lesion in 17 of 20 patients in the study (*Kinoshita et al., 2011*).

Breast conserving surgery followed by radiotherapy offer the same survival benefits as modified mastectomy in women with stage I or II breast cancer (*Veronesi et al.,2002*).

Breast conservation therapy remains the treatment of choice for early stage breast cancer patients irrespective of molecular subtype. Negative margins of excision are desirable, but the width of the negative margins does not influence outcome (**Demirci et al., 2012**)

The addition of adjuvant chemotherapy in early breast cancer improves overall survival by about 10%. Addition of hormonal treatment depends on estrogen receptor expression (**Jeorger and Thurilmann, 2013**).

The addition of neoadjuvant carboplatin to a regimen of a taxane, an anthracycline, and targeted therapy significantly increase the proportion of patients achieving a pathological complete response. This regimen seems to increase responses in patients with tripple-negative breast cancer, but not in those with HER2-positive breast cancer (**Von Micnckwitz et al., 2014**).

Oncoplastic surgery of breast cancer has generated great excitement over the past years and has become an integrated component of the surgical treatment of breast cancer. Oncoplastic surgical procedures associate the best surgical oncologic principles to achieve wide tumor-free margins with the best principles of plastic surgery to optimise cosmetic outcomes (**Franceschini et al., 2012**)

AIM OF THE WORK

This essay aims to outline the recent and different methods for diagnosis of early breast cancer as well as reviewing update treatments of early breast cancer.

Chapter (1):

Anatomy of the breast

I-Development:-

At the fifth or sixth week of fetal development, two ventral bands of thickened ectoderm (mammary ridges, milk lines) are evident in the embryo. In most mammals, paired breasts develop along these ridges, which extend from the base of the forelimb (future axilla) to the region of the hind limb (inguinal area). These ridges are not prominent in the human embryo and disappear after a short time, except for small portions that may persist in the pectoral region. Accessory breasts (polymastia) or accessory nipples (polythelia) may occur along the milk line when normal regression fails (**Bland et al., 2010**).

Each breast develops when an ingrowth of ectoderm forms a primary tissue bud in the mesenchyme. The primary bud, in turn, initiates the development of 15 to 20 secondary buds. Epithelial cords develop from the secondary buds and extend into the surrounding mesenchyme. Major (lactiferous) ducts develop, which open into a shallow mammary pit. During infancy, a proliferation of mesenchyme transforms the mammary pit into a nipple. If there is failure of a pit to

elevate above skin level, an inverted nipple results. This congenital malformation occurs in 4% of infants. At birth, the breasts are identical in males and females, demonstrating only the presence of major ducts. **(Bland et al., 2010).**

II-Gross anatomy:-

Each breast (right or left) is a rounded elevation present on the front of the upper part of the thorax, over the pectoral region. Over the centre of the breast the skin shows a dark circular area which is called the areola. In the centre of the areola there is a conical projection called the nipple **(Singh,2002).**

The adult female breast is located within the superficial fascia of the anterior chest wall. The base of the breast extends from the second rib above to the sixth or seventh rib below, and from the sternal border medially to the midaxillary line laterally. Two-thirds of the base of the breast lies anterior to the pectoralis major muscle; the remainder lies anterior to the serratus anterior muscle (fig.1). A small part may lie over the aponeurosis of the external oblique muscle **(Skandalakis et al., 2006).**

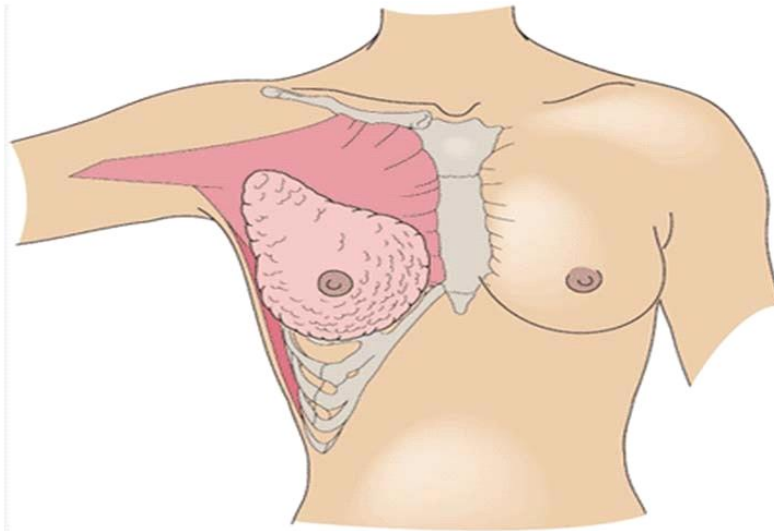


Fig. (1): The adult female breast. The upper and medial portions of the breast rest on the pectoralis major muscle, and the inferolateral portion rests on the serratus anterior (**Morrow and Khan, 2006**).

In the axillary region there is a prolongation beyond the anterior axillary line called the tail of Spencer. In adult women (i.e., after puberty), this has the shape of a drop, assuming the shape of a cone in nulliparous women and a more pendulous contour in multiparous women (**Westreich2009**)

The ligaments of Cooper are hollow conical projections of fibrous tissue filled with breast tissue, the apices of the cones being attached firmly to the superficial fascia and thereby to the skin overlying the breast. These ligaments account for the dimpling of the skin overlying a carcinoma(**Sainsbury, 2004**).