MANAGEMENT OF INFLAMMATORY BREAST CANCER

Essay
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رسالة

توطئة للحصول على درجة الماجيستير في الجراحة العامة

مقدمه من

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Hany El-Garf

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List of Abbreviations

ABCSG	: Austrian Breast and Colorectal Cancer Study Group.
ADCC	: Antibody Dependent Cell mediated Cytotoxicity.
AJCC	: The American Joint Committee on Cancer
ASCO	: The American Society of Clinical Oncology
ATAC	: Arimidex, Tamoxifen, Alone or in Combination.
BCT	: Breast conservative therapy.
BIG1-98	: Breast International Group.
CAM	: Complementary and Alternative Medicine.
CAP	: College of American Pathologists.
COX-2	: Cyclooxygenase 2.
DCIS	: Ductal Carcinoma In Situ.
DFS	: Disease Free Survival.
EOD- E	: Extent Of Disease – Extent.
EOD-S	: Extent Of Disease-S.
EREG	: EPIREGULIN: a member of the epidermal growth factor family.
FDA	: Food and Drug Administration.
FISH	: Fluorescence In-Situ Hybridization.
Flk-1	: Fetal Liver Kinase-1.
FTIs	: Farnesyl Transferase Inhibitors.
GnRH	: Gonadotropin Releasing Hormone.
H&E	: Haematoxilin and Eosin.
HD-CT	: High Dose – Chemo Therapy.
HDI	: HER-Dimerization Inhibitors.
IBC	: Inflammatory Breast Cancer.
IBCSG	: International Breast Cancer Study Group
IES	: Intergroup Exemestane Study.
ITA	: Italian Tamoxifen Arimidex.
LABC	: Locally Advanced Breast Cancer.
LHRH	: Lutinizing Hormone Releasing Hormone.
MHz	: Mega Hertz.
MMP-9	: Matrix Metallo-Proteinase-9.
MRI	: Magnetic Resonance Imagining.
MTD	: Maximum Tolerated Dose.
MTT	: Molecular Targeted Therapy.
MUC1	: A Transmembrane Mucin That Is Highly Expressed In Various Cancers.

List of Abbreviations

MVD	: Microvessel Density.
MYCN	: V-Myc Myelocytomatosis Viral Related Oncogene, Neuroblastoma Derived (Avian), also known as MYCN, Is a human gene.
NCI	: National Cancer Institute.
OFS	: Ovarian Function Suppression.
ORR	: Overall Response Rate.
OS	: Overall Survival.
PAI-1	: Plasminogen Activator Inhibitor.
PET	: Positrone Emission Tomography.
PEV	: Poussee Evolutive.
PTEN	: The Tumour-Suppressor Phosphatase with Tensin Homologue (PTEN).
RhoC-GTPase	: Ras Homolog Gene Family, Member C- Guanosine Triphosphate.
Rt-PCR	: Polymerase Chain Reaction.
SEER	: Surveillance, Epidemiology, and End Results.
SERMs	: Esteron Receptor Modulators.
SHH	: Sonic Hedgehog Protein Precursor.
TKI	: Tyrosine Kinase Inhibitor.
TNF	: Tumor Necrosis Factor.
ULABC	: Unresectable Locally Advanced Breast Cancer.
UPA	: Urokinase Plasminogen Activator.
VEGF	: Vascular Endothelial Growth Factor.
VEGFR1	: Vascular Endothelial Growth Factor Receptor1/Flt-1.

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Introduction

IBC is the most aggressive form of breast cancer. IBC incidence appears to be higher in Egypt as compared to other countries ***(Cristofdanilli et al., 2003).***

IBC occurs in approximately 2% of all breast cancers in the U.S, in Egypt it occurs in approximately 10% of all breast cancers, and exhibits a much more aggressive clinical course, and occurs with a younger age of onset ***(Loa et al., 2009).***

Inflammatory breast cancer (IBC) is the most aggressive subtype of locally advanced breast cancer, with the worst prognosis and shortest overall survival time of any variant of this disease ***(Robertson et al.,2010).***

The unique clinical and pathologic syndrome and discouraging outcome make IBC a very distinct form of breast carcinoma. The angiogenicity and propensity to invade vessels confer to IBC an extremely high metastatic potential. The percentage of infiltrating ductal carcinoma and other histological subtypes is similar to that of non-IBC ***(Jaiyesimi et al., 2002).***

Triple assessment is a multidisciplinary assessment involving radiological screening, clinical examination and biopsy. The assessment team consists of a radiologist, surgeon and pathologist ***(Fletcher et al., 2003).***

IBC is an exceptionally aggressive disease with rapid onset and distinctive clinical characteristics, including edema,

redness, dimpling of the skin, and a low frequency of occurrence of tumor masses and are easy to misdiagnose as mastitis ***(Loa et al., 2009)***.

Clinicians might not recognize IBC warning signs if women are younger, pregnant, or breastfeeding ***(Molckovsky et al., 2009).***

Symptoms are very variable and may not be present at all in occult inflammatory breast cancer. Quick onset of symptoms is typical, the breast often looks swollen and red, or "inflamed", sometimes overnight, and are easy to misdiagnose as mastitis ***(Hennessy, 2006).***

In women presenting with LABC, staging evaluations, which can include chest radiography, scentigraphy scan SS, CT, and magnetic resonance imaging (MRI), are conducted to exclude the possibility of distant metastasis before therapy is initiated ***(Robertson et al.,2010).***

With improvements in systemic treatments, locoregional management became a critical component in curative treatment. Several studies have found an association between locoregional control (LRC) and overall survival (OS) in patients with IBC treated with chemotherapy ***(Bristol et al., 2008).***

The primary goal of therapy in patients with metastatic breast cancer is palliation of symptoms and prolongation of high-quality life ***(Giordano et al., 2004)***.

Aim of the work

To spot light on inflammatory breast cancer, regarding proper clinical diagnosis, using the proper investigations, to target the ideal treatment.

Anatomy of Female Breast

Embryology and Development:

The breast develops as invagination of the 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 breast ducts and acini is developed from ectoderm, and the supporting tissue is derived from the mesenchyme ***(Van De Graaff, 2005).***

Between the 30th and 36th weeks of gestation, the solid ducts become canalized to form the lactiferous ducts. At about 38th week nipple is fromed, no involutional changes occur till 2 to 3 weeks and thereafter the breast is quiescent until 2 to 3 years prior to menarche ***(Ellis and Skandalakis, 2000).***

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).***

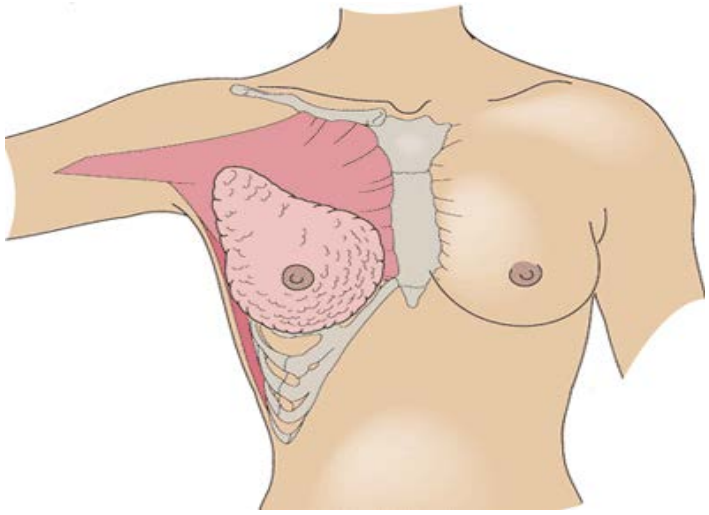

Fig. (1): The adult female breast. The upper and medial portions of the breast rest on the pectoralis major muscle, and the inferolateral portion rests on the serratus anterior ***(Morrow and Khan, 2006).***

From the upper lateral part of the gland an extension of glandular tissue passes through an aperture in the deep fascia over the axilla to enter the latter (The aperture is the foramen of Langer). This extension is called the axillary tail ***(Singh, 2002).***

The lobule is the basic structural unit of the mammary gland. The number and size of the lobule vary enormously: they are most numerous in young women. From ten to over 100 lobules empty via ductules into a lactiferous duct, of which

there are 15-20. Each lactiferous duct is lined with a spiral arrangement of contractile myoepithelial cells and is provided with a terminal ampulla, a reservoir for milk or abnormal discharges ***(Sainsbury, 2004).***

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).***

The areola contains involuntary muscle arranged in concentric rings as well as radially in the subcutaneous tissue. The areolar epithelium contains numerous sweat glands and sebaceous glands, the latter of which enlarge during pregnancy and serve to lubricate the nipple during lactation (Montgomery's tubercles) ***(Sainsbury, 2004).***

The nipple is covered by thick skin with corrugations. Near its apex lie the orifices of the lactiferous ducts. The nipple contains smooth muscle fibers arranged concentrically and longitudinally; thus, is an erectile structure which points outwards ***(Sainsbury, 2004).***

Small branching lymphatic and blood vessels course through the retromammary space between the posterior surface of the breast parenchyma and the fascia of the pectoralis major muscle; therefore the correct plane of dissection in a total mastectomy is beneath deep fascia of pectoralis muscle ***(pass, 2001).***