Update on the Management of Inflammatory Breast Cancer

An Essay

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List of Abbreviations

Abb.	Full term
ADCC	Antigen-dependent cellular cytotoxicity
AJCC	American Joint Committee on Cancer
AL	Axilliary lymphoma
Anti-VEGF	Anti-Vascular endothelial growth factor
ASCO	American Society of Clinical Oncology
ATP	Adenosine 5-triphosphate
bFGF	Basic fibroblast growth factor
CAM	Complementary and alternative medicine
CAP	College of American Pathologists
CIA	Chemotherapy-induced amenorrhea
CMF	Cyclophosphamide / methotrexate / 5-fluorouracil
CNS	Central nervous system
CT	Computed tomography
EGFR	Epidermal growth factor receptor
EOD- E	Extent of Disease – Extent
EOD	Extent of disease
EOD-S	Extent of disease-size
ER	Estrogen-receptor
FDA	Food and Drug Administration
FISH	Fluorescence in-situ hybridization
FTIs	Farnesyltransferase inhibitors
GCR	Gharbiah cancer registry
GISTs	Gastrointestinal stromal tumors
GnRH	Gonadotropin-releasing hormone
HER2	Human Epidermal Receptor Type 2

List of Abbreviations Cont...

Abb.	Full term
IBC	Inflammatory breast cancer
IBCSG	International Breast Cancer Study Group
IGF1R	Insulin-like growth factor 1 receptor
JNM	Journal of Nuclear Medicine
LABC	Locally advanced breast cancer
MoAbs	Monoclonal antibodies
MRI	Magnetic resonance imaging
MTD	Maximum Tolerated Dose
MTT	Molecular targeted therapy
MVD	Microvessel density
N/A	Not applicable
NCI	National Cancer Institute
NF-kB	Nuclear factor-kappaB
NHL	Non-Hodgkins lymphoma
OFS	Ovarian function suppression
PBL	Primary breast lymphoma
PDGFR	Platelet-derived growth factor receptor
PET	Positron Emission Tomography
PEV	Poussee Evolutive
PR	Progesterone receptor
PTEN	Phosphatase and tensin homologue
SEER	Surveillance, Epidemiology, and End-Results
TGF-α	Transforming growth factor-α
UICC	Union International Contre le Cancer
VEGF	Vascular endothelial growth factor
WO/WO	Week-on/week-off

Introduction

INTRODUCTION

Inflammatory breast cancer is a rare and aggressive form of invasive breast cancer accounting for 2.5% of all breast cancer cases. Historically, IBC is a lethal disease with less than a 5% survival rate beyond 5years when treated with surgery or radiation. In generally, woman with IBC presented a younger age are more likely to have a metastatic disease at diagnosis, have shorter survival than woman with non IBC. Although survival times have increased with multimodal therapy, they are still around 35% to 40 % and much lower than those for other breast cancer [1].

Inflammatory breast cancer is most frequent characterized by a very rapid onset of clinical signs and symptoms. Because of the possibility of mistaking IBC from a benign bacterial infection such as mastitis, it is important to note that IBC is not a true inflammatory process and is generally not associated with symptoms such as fever, localized pain, or leukocytosis. In the majority of patient with IBC, no discrete mass is palpable on clinical examination. Rapid breast enlargement and changes in the skin overlying the breast are usually the first manifestations of the disease. Early erythematous discoloration of the skin can further progress to intense red or purple color involving the entire breast. Specifically associated skin manifestation is the peau-d-orange or orange peel appearance attributed to the underlying skin edema. The rapid progression, along with

diffuse erythema of more than one-third of skin over lying the breast, distinguishes IBC From neglected LABC with skin involvement [2]. In the seven edition of American Joint Committee on Cancer staging guidelines for breast cancer, IBC is classified as stage IIIB,IIIC, or even IV, depending on nodal status and evidence of metastasis [3].

Inflammatory breast cancer is the most aggressive and fatal form of invasive breast cancer. The median overall survival duration among woman with IBC is less than 5years even with multimodality treatment option. There are few established risk factor for IBC. However, many distinguishable epidemiologic characteristics of IBC have been studied. The risk factor with the strongest association with IBC include the higher incidence evident in African American ethnicity, high body mass index, and younger age at disease onset[4].

Inflammatory breast cancer is a rare and aggressive variant of LABC. Although the disease is characterized by specific clinical manifest tation already described, it is not a specific histological sub type of mammary carcinoma. The presence of pertinent histo pathological finding in the mammary parenchyma and over lying skin, however, in conjunction with the characteristic clinical history, can allow the pathologist to suggest a diagnosis of IBC. The pathognomonic feature that distinguishes IBC from the commonly encountered LABC type is the presence of

numerous dermal tumor emboli in the papillary and reticular dermis of skin over lyingthe breast [5].

Breast tumor are categorized into specific subtypes on the basis of the basis of the presence or absence of estrogen and progesterone receptors, the level of expression of claudins, the presence and extent of amplification of the Her2oncogen, and the differential production of cytokeratin. Although IBCs may posses any combination of hormone receptors and oncogens, they are most often classified within the Her2 amplified, basal like, breast cluster and may also be low in claudin. This classification of IBC tumors is consistent with previous gene expression studies reporting that IBC tumors commonly lackER/PR and haveHer2 oncogen amplification[6]. Other characteristics of IBC tumors include high expression of the tumor suppressor P53 and over expression of the epidermal growth factor receptor (EGFR), which are both associated poor prognosis[7].

The key roles of imaging in IBC are to identify primary breast tumor and facilitate image-guided diagnostic biopsy to enable the optimal evaluation of bio marker,stage loco regional disease, diagnose distant metastases, evaluate tumor response to neoadjuvant therapy. Standard breast imaging modalities, such as mammographyand ultrasound, clinical staging and therapeutic monitoring of breast cancer, but newer modalities such as magnetic resonance imaging, hybrid positron emission

tomography/computed tomography are being used more frequently[8].

The management of IBC has substantially evolved in the past 3 decades. Surgery was the first therapeutic modality used, but it had disappointing results. The mean survival of patients treated with mastectomy alone ranged from 12 to32 months. The addition of radiotherapy improved the locoregional control rate, but it had no significant effect on survival[9]. Presently, the standard of care requires having a team of dedicated and experienced specialists (pathologist, surgeon, radiotherapist, and medical oncologist) involved in the complex management of this entity. The treatment of IBC is clearly outlined in sequence, with neoadjuvant chemotherapy representing the mainstay of treatment. Locoregional treatment includes radiotherapy with or without surgery and continues to play a major role after systemic treatment. Its sequence is greatly dependent on the quality of objective response achieved with induction chemotherapy. In the majority of cases, after optimal remission, and resolution of skin changes, patients are considered surgical candidates and a modified radical mastectomy is recommended followed by radiotherapy[10].