Clinico-Pathological Correlation of Hormone Receptors and Human Epidermal Growth Factor Receptor (HER2/neu) with Axillary Lymph Node Involvement in Females with Early Cancer Breast

Thesis

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بسم الله الرحمن الرحيم

"ويسئلونك عن الروح قل الروح من أمر ربي وما أوتيتم من العلم إلا قليلا"

صدق الله العظيم
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Sherif M. Mokhtar,

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To My family

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ADH	:	Atypical ductal hyperplasia
AIs	:	Aromatase inhibitors
ALH	:	Atypical lobular hyperplasia
ALND	:	Axillary lymph node dissection
BCS	:	Breast-conserving surgery
BCT	:	Breast-conserving therapy
BI-RADS	:	Breast imaging reporting and data system
BRCA	:	Breast cancer antigen
CC	:	Craniocaudal
CHF	:	Congestive heart failure
CISH	:	Chromogenic in situ hybridization
CT	:	Computed tomography
DCIS	:	Ductal carcinoma in situ
DFS	:	Disease-free survival
ECD	:	Extracellular domain
EGFR	:	Epidermal growth factor receptor
ELISA	:	Enzyme-linked immuboabsorbent assays
ER	:	Estrogen receptor
FISH	:	Fluorescence in situ hybridization
FNA	:	Fine needle aspiration
HER	:	Human epidermal growth factor receptor
HT	:	Hormonal therapy
IHC	:	Immunohistochemistry
ILC	:	Invasive lobular carcinoma
ITC	:	Isolated tumor cells
LCIS	:	Lobular carcinoma in situ
LHRH	:	Leutinizing hormone release hormone
LVI	:	Lympho-vascular invasion
MAb	:	Monocloncal antibody
MLO	:	Mediolateral oblique
MRI	:	Magnetic resonance imaging
MRM	:	Modified radical masectomy
NOS	:	Not otherwise specified
NSABP	:	National surgical adjuvant breast and bowel project
OCP	:	Oral contraceptive pills
PAI-1	:	Plasminogen activator inhibitor type-1
PET	:	Positron emission tomography

PR	:	Progesterone receptor
RM	:	Radical masectomy
RS	:	Recurrence score
RT	:	Radiation therapy
RT-PCR	:	Reverse transcriptase polymerase chain reaction
SBR	:	Scarf-Bloom-Richardson
SD	:	Standard deviation
SERM	:	Selective estrogen receptor modulator
SLNB	:	Sentinel lymph node biopsy
SN	:	Sentinel node
SPF	:	S-phase fraction
T	:	Primary tumor
TDLU	:	Terminal duct lobular unit
TFGα	:	Transforming growth factor-alpha
TFGβ	:	Transforming growth factor-beta
UPA	:	Urokinase-type plasminogen activator

ABSTRACT

In women with early breast cancer (stage I, stage II), the tumor expression of HER2/neu and hormone receptors (ER, PR), which are emerging prognostic factors, could not be related to the axillary lymph node status, whether positive or negative node; table (11). And this is consistent with the clinical observations in the literature. And the data from literature suggest that HER2/neu is associated with more aggressive tumor, but its use as a determining factor in selecting the line of adjuvant therapy is still limited by the varying methods employed to detect over-expression. While the axillary lymph node status is the most consistent prognostic factor used in adjuvant therapy decision making. Patients with positive lymph nodes are offered adjuvant therapy. Meanwhile, the prognostic significance of estrogen or progesterone receptors is limited. Its optimal use is as a predictive factor for the benefit of adjuvant tamoxifen therapy. As demonstrated in the literature, all hormone receptor-positive women who warrant adjuvant systemic therapy should receive hormonal therapy unless otherwise contraindicated.

Keywords:

HER2/neu
ER, PR receptors
Early female breast cancer
Clinico-pathological correlation
Axillary lymph nodes

INTRODUCTION

Introduction

Breast cancer is the most common cancer and the second most common cause of death from cancer in women. Because of the high frequency of the disease and the esthetic and symbolic value invested in the breast, breast cancer has always been a source of severe distress to patients and their families. For the same reasons, breast cancer research has increased dramatically during the last 2 decades, resulting in extraordinary progress in our understanding of the disease and in new, more efficient and less toxic treatments. Furthermore, the diffusion of knowledge, the medical advancements, and the increased public awareness have led to earlier diagnosis at stages usually amenable to complete resection and potential cure of the disease ***(von Smitten, 2000).***

Over the past few decades, breast cancer management has undergone significant changes characterized by less aggressive approaches to diagnosis and treatment. Mammogram and ultrasound or stereotactic biopsies have supplanted clinical diagnosis and surgical biopsy for the diagnosis; breast-conserving surgery (BCS) and sentinel lymph node biopsy (SLNB) have successfully replaced the more aggressive radical mastectomy(RM) and axillary lymph node dissection (ALND) ***(Blichert-Toft, 2000).***

These changes are the results of a century-long experience whereby different models for the disease have been proposed and tested. RM, introduced by Halsted at the end of the last century, was based on the centrifugal model of tumor spread, according to which cancer spread starts locally then moves to the lymphatics and only then invades distant organs. Despite increasingly radical procedures, most patients relapsed with systemic disease ***(Blichert-Toft, 2000).***

New paradigms appeared to palliate the deficiency of this model. Both the systemic and the spectrum models acknowledge the role of the blood stream in tumor dissemination independent of lymphatic invasion, but they differ in their explication of the relationship between tumor size and distant metastasis ***(Edwards et al., 2000).***

The systemic model considers breast cancer a systemic disease from its inception, while the spectrum model views breast cancer as a progressive disease in which invasion and metastases are a function of tumor growth and biological transformation. In addition, this model acknowledges that the disease may manifest over a spectrum of biological behaviors, with tumors that are metastatic from the beginning and others that may reach large sizes without dissimination ***(Whitworth et al., 2001).***

Modern trials comparing different forms of loco-regional control for patients at the same stage of disease show that variations in local treatment do not result in differences in long-term survival, validating the first premise of these models regarding the inadequacy of local approaches to control the disease in the absence of systemic therapy. In addition, screening mammography results in early detection of breast cancer (average size 1.4 cm vs 2.2 cm for tumors clinically detected) and is associated with a 25% decrease in the mortality rate for breast cancer, thus lending credibility to the spectrum model. This model stresses the importance of both local and systemic treatment ***(Jacobson et al., 1995).***

ALND remains one of the mainstays of breast cancer management because clinical, imaging, or biological methods are insufficient to reliably define nodal status, the most reliable predictor of final outcome. Furthermore, ALND allows local control of the disease and may also improve survival. However, the extent of axillary dissection is still debated. Knowing that the procedure has risks of chronic morbidity in terms of arm mobility and lymphedema, the question is not a trivial one. Results from several prospective studies show that 10 nodes or more should be removed and found negative before declaring the axilla stage N0. This involves a level I dissection and, usually, a level II dissection ***(Lichtenstein et al., 2000).***