

**STROMAL MAST CELLS IDENTIFICATION IN
INVASIVE BREAST CARCINOMA
(IMMUNOHISTOCHEMICAL AND CYTOLOGICAL
STUDY)**

THESIS

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ABSTRACT

Introduction: Breast cancer is the most frequent malignant tumor of women worldwide, with increasing incidence rates. The assessment of prognostic factors, in order to provide a prediction of outcome, has become an essential part of the histopathologist's role in the handling and histological reporting of invasive breast carcinomas. The role of the immune system during cancer development is complex involving extensive reciprocal interactions between genetically altered cells, immune cells, and the neoplastic microenvironment. Studies on the role of mast cells in cancer have given contrasting results, research on breast cancer was specifically of importance, because some aspects of its carcinogenesis, such as the diversity of the hormonal component, differ greatly.

Material & methods: Fifty cases of breast cancer were collected randomly as tissue sections and cell block prepared material. The cases were stained by Haematoxylin and Eosin, ckit (CD 117) immunostaining and toluidine blue special stain for mast cells detection followed by their quantitative evaluation.

Results: The majority of cases presented in the age group 41-50 years representing (36%) of the total count of cases. This study revealed that the most common type was invasive duct carcinoma NOS representing (84%) of the cases. Most were those with maximal dimension were within the range between 2cm up to less than 5 cm compromising (68%) of cases, the majority of cases the majority of cases (62 %), showed positive nodal status. No statistical correlation was found between mast cells and clinicopathological factors of breast cancer. On the other hand, there was significant correlation between nuclear grade and ckit (CD117) expression.

Key words: Breast Carcinoma, Mast cells, ckit, Toluidine-blue

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LIST OF ABBREVIATIONS

AJCC: American Joint Committee on Cancer

ASR: Age-Standardized Incidence Rates

ATM: Ataxia Telangiectasia mutant gene

BBD : Benign Breast Disease

BMD: Bone Mineral Density

BRCA1: Breast Cancer Gene 1

BRCA2:Breast Cancer Gene 2

ESR1: Estrogen receptor alpha gene

FDA: Food and Drug Administration

GCDFP-15: Gross Cystic Disease Fluid Protein-15

HER2: Human Epidermal Growth Factor Receptor 2

HRT: Hormone replacement therapy

IGF-I: Insulin-Like Growth Factor-1

MECC: Middle East Cancer Consortium

OCs: Oral contraceptive pills

PTEN : Phosphate and Tensin homology

TAA : Tumor-Associated Antigen

TAMs: tumorassociated macrophages

TDLU: Terminal Duct-Lobular Unit

WHO: World Health Organization

Introduction

INTRODUCTION

Breast cancer is the most frequent malignant tumor of women worldwide, with increasing incidence rates. The most widely cited reason for the global increase in breast cancer is the "Westernization" of the developing world **(American Cancer Society, 2007)**.

The assessment of prognostic factors, in order to provide a prediction of outcome, has become an essential part of the histopathologist's role in the handling and histological reporting of invasive breast carcinomas **(Fodor, 2007)**.

Standard treatment modalities have improved the overall outlook and quality of life for women with breast cancer; however, the fact that 40% still succumb to disease highlights the need for new prognostic indicators and therapeutic approaches **(DeNardo & Coussens, 2007)**.

The role of the immune system during cancer development is complex involving extensive reciprocal interactions between genetically altered cells, adaptive and innate immune cells, their soluble mediators and structural components present in the neoplastic microenvironment **(De Visser & Coussens, 2006)**.

The accumulation of mast cells has been associated with enhanced growth and invasion of several human cancers, by several mechanisms as promoting tumor angiogenesis **(Ribatti et al., 2001)**.

On the other hand, mast cells infiltration has been associated with good prognosis in some types of cancer, as breast cancer. This may be related to many factors, as secreting large numbers of amines that may influence breast

carcinoma cells to invade and metastasize, or possibly by producing products as interleukin-4 that may induce apoptosis of the breast cancer cells **(Dabiri et al., 2004)**.

Therefore, as studies on the role of mast cells in cancer have given contrasting results, research on breast cancer was carried out in order to contribute to the clarification of their role. Breast cancer was specifically of importance, because some aspects of its carcinogenesis, such as the diversity of the hormonal component, differ greatly **(Rovere et al., 2007)**.

Detection of mast cells can be undergone by various staining techniques and immunohistochemical methods. Cytoplasm of mast cells contains granules (metachromatic) composed of heparin and histamine. Toluidine blue should stain mast cells red-purple (metachromatic staining) and the background blue (orthochromatic staining). Immunohistochemistry can be applied by using antibody to cKIT (CD117), a transmembrane tyrosine kinase acting as a type III receptor for MC growth factor **(Liu et al., 2002)**.

Aim Of The Study

AIM OF THE STUDY

*Collection of a random number of invasive breast cancer cases, with their full clinical and histopathological data including age, tumor size, grade, histological subtype, nodal status, and others.

*Studying the cases prepared as formaline fixed paraffin embedded (FFPE) primary tumor samples, as well as cytology samples obtained from fresh specimens with paraffin blocks processing.

*Detection of mast cells within breast stroma using toluidine blue and cKIT antibody , and their quantitative evaluation.

*Correlation between presence or absence of stromal mast cells and their quantity if present, to other clinical and pathological features, and to prove or disprove their prognostic significance.

Review Of Literature