Immunohistochemical expression of EGFR in triple-negative breast cancer and its correlation with clinicopathological characteristics of these tumors

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Abstract

Background:

Triple negative breast carcinomas (TNBCs) are a group of primary breast tumors with aggressive clinical behavior that have no targeted therapy at present. EGFR expression has recently come into focus as an index for molecular targeting therapy. Histologic sections that included variable subtypes and grades of TNBCs were studied by immunohistochemistry with EGFR, using a standard avidin–biotin–peroxidase system.

Results: Twenty two cases showed variable positive reactivity for EGFR (55% of total cases).

Conclusions: the level of EGFR expression was relatively high as most studies stated, and agreed with most studies about the statement that EGFR expression is associated with worse prognosis.

Key Words: Triple, negative, TNBC, EGFR.

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LIST OF ABBREVIATIONS

- **BLBC:** Basal-like Breast Cancer.
- **BPBC:** Basal Phenotype Breast Cancer.
- **BRCA-1:** Breast Cancer 1.
- **BRCA-2:** Breast Cancer 2.
- **CK5/6:** Cytokeratin 5/6.
- **CSCs:** Cancer Stem Cells.
- **DCIS:** Ductal Carcinoma In Situ.
- **ECD:** Extracellular Domain.
- **EMT:** Epithelial to Mesenchymal Transition.
- **EGFR:** Epidermal Growth Factor Receptor.
- **ER:** Estrogen Receptor.
- **FDG-PET:** Fluorodeoxyglucose- Positron Emission Tomography.
- **FISH:** Fluorescent In Situ Hybridization.
- **GMP:** Glomeruloid Microvascular Proliferation.
- **HER-2/neu:** Human EGFR Related -2/neural.
- **HR:** Hormone Receptor.
- **IHC:** Immunohistochemistry.
- **MBCs:** Medullary Breast Carcinomas.
- **NR:** Nuclear Receptor.
- **NSCLC:** Non-Small Cell Lung Cancer.
- **OS:** Overall Survival.
- **PARP:** Poly(adenosine diphosphate-ribose) Polymerase.
- **pCR:** pathologic Complete Response.
- **PFS:** Progression- Free Survival.
- **PMRT:** Post-Mastectomy Radiation Therapy.
- **PR:** Progesterone Receptor.
- **TDLU:** Terminal Duct Lobular Unit.
- **TKIs:** Tyrosine Kinase Inhibitors.

INTRODUCTION

Breast cancer is the most common female cancer, worldwide, more than a million women are diagnosed every year, however despite this increase, the mortality rate is declining, this is due to combination of factors including early diagnosis and effective treatment ***(Keshtgar et al., 2010).***

In the national cancer institute of Egypt, in the period between 2003 and 2004, breast cancer came as number one in ranking of malignant tumors constituting 17.50% of total malignancies ***(Mokhtar et al.,* 2007)**.

Breast cancer is a common but very diverse disease with considerable survival heterogeneity. An ongoing challenge is to find improved methods of identifying and classifying groups of tumors with differing biological behaviours or responsiveness to specific therapies ***(Tavassoli et al., 2003).***

Triple negative breast carcinomas (TNBCs) are a group of primary breast tumors with aggressive clinical behavior. Most TNBCs possess a basal phenotype (BP). The importance of recognizing these tumors came to light largely as the result of gene expression profiling studies that categorized breast cancer into 3 major groups. Two of these groups are defined by their respective expression of estrogen receptor and HER2. TNBCs represent a third group and are defined by negativity for hormone receptors and HER2 ***(Diaz et al., 2007).***

Epidermal growth factor receptor (EGFR) is a member of the ErbB family, a family of tyrosine kinase receptors with growth-promoting effects ***(Rogers et al., 2005).***

EGFR expression in breast cancer has been investigated in a variety of studies whose results suggest that a relation to aggressive tumor behavior remains controversial, but that expression might be an indicator of less favorable response to anticancer agents, on the other hand, EGFR expression has recently

come into focus as an index for molecular targeting therapy; thus knowledge of a patient's immunohistochemical EGFR expression might be useful information to treat triple-negative breast cancer ***(Tadahiro et al., 2010).***

AIM OF WORK

- Histopathological studying of triple-negative breast carcinomas.
- To evaluate immunohistochemically the expression of EGFR in triple-negative female breast cancer and it's relation to available clincopathologic features.

EPIDEMIOLOGYAND RISK FACTORS OF BREAST CANCER:

Breast cancer ranks first among cancers affecting women throughout the world. Estimates suggest that more than 1,050,000 new breast cancer cases are added worldwide annually, with nearly 580,000 cases occurring in developed countries and the remainder in the developing countries ***(Stewart et al., 2003).*** Breast cancer accounts for 23% of cancer cases, it is estimated that approximately 1 in 11 women will suffer from the disease at some point in their lifetime, there were over 200,000 cases diagnosed in the U.S. alone in 2005, and the incidence of new cases continues to rise worldwide ***(Parkin et al., 2005).*** Triple negative breast carcinoma (TNBC) represents 10-17 % of all breast cancers ***(Katerina et al., 2009).***

In Egypt, ***Abd El-Bar et al., (2007),*** recorded that breast cancer was the most frequent cancer among Egyptian females, accounting for 17.5% of all incident cancers and 35.7% of all newly diagnosed female cancers over a period of three years (2000-2002).

Race is regarded as a prognostic factor in a sense that non-Hispanic black women with late-stage triple-negative breast cancer has the poorest survival of any comparable group, with a 5-year relative survival of only 14%, and this is much lower than other race groups with the same tumour; the 5-year relative survival is 36% for non-Hispanic white women and 37% for Hispanic women with late-stage triple-negative breast cancer. It is also much lower than the same race group, non-Hispanic black women, diagnosed at late stage with other breast cancers, for which the 5-year relative survival is 49% ***(Tischkowitz et al., 2007).***

Although many epidemiological risk factors have been identified, the cause of any individual breast cancer is often unknowable. No etiology is known for

95% of breast cancer cases, while approximately 5% of new breast cancers are attributable to hereditary syndromes ***(Giordano et al., 2004).***

Worldwide, breast cancer is the fifth most common cause of cancer death (after lung cancer, stomach cancer, liver cancer, and colon cancer). In 2005, breast cancer caused 502,000 deaths (7% of cancer deaths; almost 1% of all deaths) worldwide. Among women worldwide, breast cancer is the most common cause of cancer death ***(Espey et al. 2007).***

The number of cases worldwide has significantly increased since the 1970s, a phenomenon partly blamed on modern lifestyles in the Western world. Because the breast is composed of identical tissues in males and females, breast cancer also occurs in males, though it is less common ***(Espey et al. 2007).***

Risk Factors:

1- Atypia or cancer on previous biopsy:

■Atypical ductal hyperplasia (ADH).

■ Atypical lobular hyperplasia (ALH).

■ Lobular carcinoma in situ (LCIS).

■ Previous history of ductal carcinoma in situ (DCIS).

■Previous history of invasive breast cancer. ***(Chen et al., 2002).***

2- Thoracic Radiation Before Age 30:

■ e.g., Hodgkin's.

■ Infant thymus radiation.

■ Frequent fluoroscopy for TB.

■ Multiple x-rays for scoliosis. ***(Goss et al., 1998).***

3- Family History—Three Generations Maternal and Paternal*:*

■ Known or suspected gene mutation

■ Early age onset <40