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Tumour Markers in Breast Cancer

P. S. Aishwariya

Saveetha Dental College, Chennai

Abstract: ***Tumor markers are substances that are produced by cancer cells or by other cells of the body in response to cancer or certain benign conditions, however, they are produced at much higher levels in cancerous conditions. These substances can be found in the blood, urine, stool, tumor tissue, or other tissues or bodily fluids of some patients with cancer. Most tumor markers are proteins. Some tumor markers help determine the effective treatment while some are prognostic which denotes that they determine the outcome of the cancer. Tumor markers are measured in the management of breast cancer patients for Early detection. blood tumor markers such as CA 15-3 are useless for this detection because of a low sensitivity. Proteomics profiling has recently been investigated using blood or nipple aspirate fluid for the detection. This article mainly focuses on the tumor markers involved in breast carcinoma and their prognostic patterns.***

Keywords: cancer, knowledge, markers

1. Introduction

HER2 is a special protein on the surface of cells that is both prognostic and determines the treatment that should be pursued. Though not true tumor markers, the estrogen receptor(ER) and the progesterone receptor(PR) determine which treatment to be administered.CA15-3 is produced by normal breast cells and an increase in cell numbers will result in elevated levels, however increases in this marker can also be caused by other non-cancerous conditions. Other makers include Ki67, up A, PAI-1 and CEA. The list of tumor markers involved in breast carcinoma are as follows:

- CA15-3/CA27.29
- Estrogen receptor (ER)
- Progesterone receptor (PR)
- HER2/neu
- Urokinase plasminogen activator (uPA) and plasminogen activator inhibitor

CA15-3/CA27.29

It is found on the surface of many types of cancer cells and shed into the blood stream Elevated CA15-3, in conjunction with alkaline phosphatase (ALP), was found to be associated with an increased chance of early recurrence in breast cancer. CA15-3 and associated CA27.29 are different epitopes on the same protein antigen product of the breast cancer-associated MUC1 gene. CA27.29 has enhanced sensitivity and specificity and has therefore surpassed CA15-3 as a serum tumor marker. CA27.29 is elevated in 30% of patients with low-stage disease and 60 to 70% of patients with advanced-stage breast cancer. Neither of these markers is recommended by physician organizations for use in the screening or detection of breast cancer. This is in part due to the elevation of the markers in benign conditions including: breast, liver and kidney disorders and other cancers. The CA15-3/CA27.29 test result serves as a baseline to compare with future measurements. During therapy, serial CA 15-3 results may be used to monitor response to therapy. Increasing results may be indicative of progressive disease, decreasing results may be indicative of response to therapy and constant results may be associated with stable disease.

HER2/neu

Receptor tyrosine protein kinase erbB-2 also known as CD340 or Proto -oncogene Neu is a protein that in humans is encoded by the ERBB2 gene. The ERBB2 gene is also frequently called HER2 (human epidermal growth factor receptor 2). Amplification or over expression of this oncogene has been shown to play an important role in the development and progression of certain aggressive types of breast cancer. In recent years the protein has become an important biomarker and target of therapy for approximately 30% of breast cancer patients. In about 1 of every 5 breast cancers, the cancer cells make an excess of HER2 due to a gene mutation. This is a gene mutation that occurs only in the cancer cells and is not a type of mutation that can be inherited from a parent.HER2-positive breast cancers tend to be more aggressive than other types of breast cancer. They are also less responsive to hormone treatment. However, treatments that specifically target HER2 are very effective. These include, Trastuzumab, Lapatinib.

Estrogen Receptor (ER)/Progesterone Receptor (PR)

ER and PR are a group of proteins activated by the hormone estrogen. It is a DNA-binding transcription factor.Estrogen receptors (ER) and progesterone receptors (PR; also called PgR) may be found in breast cancer cells. Cancer cells with these receptors depend on estrogen and related hormones, such as progesterone, to grow. Estrogen and progesterone influence many hormonal functions in women, such as breast development.

If breast cancer cells have estrogen receptors, the cancer is called ER-positive breast cancer. If breast cancer cells have progesterone receptors, the cancer is called PR-positive breast cancer. If the cells do not have either of these two receptors, the cancer is called ER/PR-negative. About two-thirds of breast cancers are ER and/or PR positive.

The expression of the hormone receptors ER and PR in a patient's breast cancer is an example of a weak prognostic but strong predictive biomarker. If a patient's tumor expresses ER and/or PR, as seen in approximately 70% of invasive breast cancers, we can predict that this patient will likely benefit from endocrine therapy such as tamoxifen.

Urokinase Plasminogen Activator & Plasminogen Activator Inhibitor

The urokinase plasminogen activator (uPA) system consists of the serine protease uPA, its glycolipid-anchored receptor, uPAR and its 2 serpin inhibitors, plasminogen activator inhibitor-1 (PAI-1) and plasminogen activator inhibitor-2 (PAI-2).Plasminogen activator inhibitor-1 (PAI-1) also known as endothelial plasminogenactivator inhibitor or serpin E1 is a protein that in humans is encoded by the *SERPINE1* gene.

PAI-1 is a serine protease inhibitor (serpin) that functions as the principal inhibitor of tissue plasminogen activator (tPA) and urokinase (uPA), the activators of plasminogen and hence fibrinolysis . It is a serine protease inhibitor (serpin) protein (SERPINE1).

Recent findings suggest that the uPA system is causally involved at multiple steps in cancer progression. In particular, uPA has been implicated in remodeling of the extracellular matrix, enhancing both cell proliferation and migration and modulating cell adhesion. Consistent with its role in cancer progression, multiple groups have shown that high levels of uPA in primary breast cancers are independently associated with adverse outcome. Paradoxically, high levels of PAI-1 also correlate with poor prognosis in patients with breast cancer.

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