Molecular Subtypes and Clinical Outcomes of Breast Cancer

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Breast cancer is a significant cause of worldwide morbidity and mortality in females (1). A major challenge in the diagnosis and treatment of breast cancer is its heterogeneity, because individual breast tumours can exhibit tremendous variations in clinical presentation, disease aggressiveness and treatment response (2). Breast cancers can also display strikingly distinct clinical characteristics in different patient and ethnic populations (3). For example, in Caucasian populations, most breast cancers occur in post-menopausal women at a mean and median age of 60 and 61 years respectively (4). In contrast, a bimodal pattern of incidence, beginning at age 40 is seen in both Asian and African population such as those seen in Singapore and Kenya (5-8).

Gene expression profiling in tumour tissues suggest that breast cancers may be subdivided into two subtypes consisting of two estrogen receptor (ER) – positive types, (Luminal A and Luminal B) and three (ER) negative subtypes. (Human epidermal growth factor receptor 2 – expressing, Basal like (ER–ve PgR-ve and Her2-ve) triple negative, "Normal like" – Un classified. All these subtypes have distinctive clinical outcomes (9-11).

Specifically, luminal A tumours, characterized by positive ER/PgR and negative HER2, show the most favourable clinical features among the five subtypes. Luminal B tumours express HER1/HER2 in addition to ER/PgR, show less favourable clinical outcomes compared with luminal A tumours. Basal-like tumours are characterized by the expression of cytokeratins 5/6 (CK 5/6) and CK17 and are prevalent in patients with BRCA1 mutations (11). Basal like and HER2 – over-expressing groups both are ER/PR – negative and have been associated with poor clinical features and survival.

Data suggests that molecular profiles in breast cancer are generally fixed at inception (12). Therefore, exposures that influence the risk of developing breast cancer might be related to the tumour. Molecular profiles later affect the biology and clinical behaviour of the tumours that arise.

Some early work has started in earnest at both the AKUH(N) and Kijabe Hospitals to try and stratify our breast cancer patients to those mentioned subtypes to help in both diagnosis and treatment. The limiting factors are small numbers of patients expense to undertake the tests and lack of both internal and external validation (13).

We should feel encouraged to carry on the work and give our patients individualized breast cancer care based on their known molecular subtypes that well and clearly determine their clinical behaviour and outcome.

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