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Editorial

Breast Cancer - Changing Role of the Pathologist

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Breast cancer is the most common malignancy in women, leading to a significant burden on the society. Since, early detection is the strongest predictor of overall survival; screening program by mammography was initiated and has already gained worldwide acceptance. For such programs to succeed, multidisciplinary team is indispensable. In the multidisciplinary team, the pathologist is a central role player providing prognostic data as well as data that helps in selecting a targeted therapeutic strategy. In Bahrain, it is obvious that there is a dire need to initiate a nationwide breast-screening program, as breast cancer is a common problem that seems to affect younger age group.

Breast cancer is a leading killer in women. Breast cancer mortality is second to mortality from cancer of the lung and bronchus. Overall one in ten women will develop breast cancer in their lifetime[1].

Early detection is the best predictor of survival. Therefore, screening program by mammography was initiated and has already gained reasonable worldwide acceptance. For a breast-screening program to succeed, a multidisciplinary team effort is mandatory. A team of healthcare specialists need to coordinate their efforts in order that every single woman assessed for mammographic abnormality gets a timely state of the art standard of care. Patients will thus receive prompt medical care from each discipline, where all services are coordinated. A multidisciplinary team in any centre where breast screening is up and running is usually constituted of a radiologist, cytopathologist, breast surgeon, pathologist, radiation oncologist, oncology counseling nurse, liaison officer, statistician and a social worker[2].

The role of the pathologist in breast cancer is not merely as a diagnostician as it once was decades ago. Nowadays, the pathologist's role far exceeds that; where the pathologist is also required to give various prognostic indices and data that help the oncologist predict the prognosis of an individual patient as well as tailoring a therapeutic regimen that is compatible with the biological characteristics and behavioral potential of that particular cancer.

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The prognosis is measured by a number of indices which were devised to predict as much as possible the patient's prognosis individually. The most widely acceptable is the Nottingham Prognostic Index, where the pathologist is in a position to calculate the index from the three strongest independent prognostic factors; namely: tumor size, tumor grade and lymph node stage. Accordingly, the patient would be assigned to either good, middle or poor prognostic group. Such groupings were found to have 80, 20-80, and 20% five-year survival respectively [1].

Therapeutically, the pathologist's role is to assess the tumor for the expression of estrogen and progesterone receptors, as well as the Her-2/neu status. These are routinely assessed immuno-histochemically with semi-quantitative analysis of the expression and intensity of expression of both steroid hormones (estrogen and progesterone receptors). Steroid hormone positive tumor responds to hormonal manipulative therapy such as tomaxifen.

Her-2/neu (c-erbB-2) is one of the best characterized human epidermal growth factor receptor. Breast cancer patients with amplification of the Her-2/neu gene (positive Her-2/neu status) usually have aggressive tumors and poor prognosis.

The most widely accepted method of determining Her-2/neu status is by immuno-histochemistry, followed by fluorescent in-situ hybridization (FISH) technique in equivocal cases. This can usually be reliably done on formalin-fixed, paraffin-embedded tumor tissue.

Her-2/neu over-expressing tumor will usually respond to herceptin (trastuzumab) therapy. Herceptin is a monoclonal antibody raised against Her-2/neu. This is the prototype of targeted therapy[3,4].

The use of molecular and immuno-histochemical techniques is thus providing insights that will allow us to tailor the management of patient with breast cancer. Tests for BRCA1 and BRCA2 genes to determine familial breast cancer is also available but is only incorporated as part of routine practice in some centers.

Vast data are available about breast cancer. It is getting increasingly clear that breast cancer is not a simple disease, where one treatment protocol suits all. It is rather a complex disease with an interplay of myriads of factors, which makes it mandatory to customize treatment to each individual patient. It is no longer " one size fits all" approach when it comes to breast cancer management. Targeted therapy is now the way forward and herceptin therapy exemplifies the first of such therapies.

Advances in research of breast cancer "signaling pathways" will enable the production of therapeutic agents targeting at least some molecules involved in angiogenesis, proliferation, invasion, resistance, metastasis, and survival.

This paves the way for the future of breast cancer therapeutics, where, recent advances in genomics, particularly DNA-sequencing and DNA-chip technology are set to make it possible to identify small molecules. Such molecules are then "targeted" by various therapeutic approaches. In addition, differential gene expression profiling

using microarrays is being used to compile the genetic pattern of breast cancer. This will hopefully contribute to a more accurate cancer classification [5].

In Bahrain, cancer of the breast seems to affect younger women, they present with larger primary tumors as compared to those in the developed world, where breast screening is well established. Familial breast cancer is seen as well as aggressive and rare tumors.

Future research is required to elucidate further such observations and to establish the variety of factors of importance in this region. Moreover it is essential to organize a multidisciplinary team, which has the capacity and the authority to run a national breast-screening program. Instituting these measures will help reduce breast cancer mortality in the long run.

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