Triple-Negative Breast Cancer; Future Treatment in Limited Resource Centers

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Editorial

Breast cancer, a malignant disease that develops in the milk ducts (duct carcinoma) or glands (lobular carcinoma), has an immense global impact. It is the second most common cancer worldwide after lung cancer, the fifth most common cause of cancer death, and the leading cause of cancer death in women. The global burden of breast cancer exceeds all other cancers and the incidence rates of breast cancer are increasing [1]. In the United States, incidence rates of breast cancer among women vary substantially by racial/ethnic group [2-3].

The majority of breast cancer deaths occur in low- and middle-income countries, where awareness is limited and delayed admission is common [4]. The epidemiology of breast cancer is different in the Middle East. In many countries in the region, such as Iran, Turkey, and Pakistan, women diagnosed with breast cancer are almost 10 years younger than those diagnosed in western countries. Furthermore, in the Middle East, most women diagnosed with breast cancer are diagnosed with advanced stages of the disease [5]. In Yemen, the incidence of breast cancer disease is rising and many patients present with advanced stages due to delay in admission and they are in average one decade younger than their western counterparts at the first presentation [6].

Molecular methods by genomic techniques have identified different subtypes of breast cancer. These molecular classification of breast cancer based on gene expression profiles segregates breast cancer into 5 subtypes (1) luminal A, (2) luminal B, (3) basal, (4) HER2 and (5) normal like type (Table 1).

Gene expression profiling and molecular pathology have revealed that BC naturally divides into luminal A and B, HER2-enriched, basal-like and claudin-low subtypes. The basal-like BC is tumor that possesses characteristics of breast basal epithelial cells at the gene level [7].

The triple-negative breast cancer (TNBC) is defined by lack of protein expression of the estrogen receptor (ER) and progesterone receptor (PR) and the absence of tyrosine kinase human epidermal growth factor receptor 2 (HER 2) [8]. TNBC is characterized by up regulation of cytokeratins 5, 14, and 17 and increase of the epidermal growth factor receptor (EGFR). Triple-negative breast cancer (TNBC) accounts for approximately 20% of breast cancer [9].

TNBCs are typically aggressive, invasive, grade III with high rates of mitotic division and with 50% high rate of P53 mutation [10], which is directly responsible for metastatic to visceral organs, distant recurrence, and death among breast cancer patients. The prognosis is poorer than other breast cancer subtypes, regardless of the stage of disease at the time of diagnosis and associated with decreased progression-free survival (PFS) and overall survival after surgery or after recurrence [11,12].

The treatment of TNBC has the potential to drastically improve in the future. Triple negative breast cancer have a good initial response to chemotherapy, particularly anthracycline and taxane-based therapy such as AC [doxorubicin, cyclophosphamide] followed by T [docetaxel], or TAC [docetaxel, doxorubicin, cyclophosphamide], and nonanthracycline-based regimens such as TC [docetaxel, cyclophosphamide]. Ixabepilone (Ixempra) was the first epothilone to be approved by the USFDA for the treatment of patients with locally advanced or metastatic breast cancer in combination with capecitabine (Xeloda) after failure of an anthracycline and a taxane and as monotherapy after failure of an anthracycline, taxane, and capecitabine [13]. The protocols with platinum compounds for neoadjuvant therapy are being tested in some clinical trials. Other studies noted VEGF introduced in treatment of TNBC patients compared to non-TNBC, and the antiangiogenic agent bevacizumab is being studied in combination with several chemotherapy agent in clinical trials [14]. Many newer therapeutic approaches are under investigation in TNBC. Most of these chemotherapeutic and targeted therapies are investigated to exploit a proliferative phenotype either directly or indirectly (Table 2).

The risk factors like age, race, premenopausal status, hormonal contraceptive use, multiparity, late stages and high grade diseases were associated with TNBC. In the last 10 years there are no first-line therapies specific for TNBC. The researchers are working on different aspects researches, such as Receptors, Gene level, Signaling pathway, Immunomodulatory, and others.

Future treatment in limited resource center countries need urgent improvement of breast cancer awareness especially in patients with TNBC, because the rising of breast cancer mortality rates among triple negative are expected to be greatest in these countries due to absence of

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Receptor Status</th>
<th>5-Years OS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal-like/Triple negative (20%)</td>
<td>ER/PR, HER2</td>
<td>63-73</td>
</tr>
<tr>
<td>Luminal A (50%)</td>
<td>ER/PR, HER2</td>
<td>85-95</td>
</tr>
<tr>
<td>Luminal B (15%)</td>
<td>ER/PR, HER2</td>
<td>70-80</td>
</tr>
<tr>
<td>HER2 neu expression (07%)</td>
<td>HER2, ER/PR</td>
<td>55-65</td>
</tr>
<tr>
<td>Normal like (06%)</td>
<td>ER/PR, HER2 (+/-)</td>
<td>84-94</td>
</tr>
</tbody>
</table>

Table 1: Summary of breast cancer molecular subtypes [7].

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genetic expression study in some countries and unavailability of target therapy. It is hoped that insights into the biology of triple negative breast cancer will lead to improvement of therapeutic strategies and better outcomes of patients with TNBC.

References