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Chapter 1

Introductory Chapter: Carcinogenesis and Clinical Reflections

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http://dx.doi.org/10.5772/intechopen.79622

1. General overview on breast cancer treatments

Breast cancer ranks fifth in cancer-related deaths among women. Therefore, the selection of systemic and local treatments influences the prognosis. They show different signal pathway and genetic differentiation. Besides ER, PR, and HER-2 receptor levels used in practice, cytokeratin, EGFR, germ line mutations, and mesenchymal markers currently bring many treatment approaches into question. This shows the presence of factors that have not yet been fully understood. Hence, as new pathways, mutations, and different chemotherapeutic agents gain currency in the ongoing follow-up of each patient, clinicians are alienated from the standard treatment approach. In this chapter, local treatment options, early and advanced breast cancer treatments, drug resistance factors, alternative treatments, and palliative care have been addressed.

1.1. Local and systemic therapies

Breast cancer has been described in a sequential algorithm based on progressive disease course, beginning from neoadjuvant treatments. Approach to breast cancer as a systemic disease starting from the diagnosis phase extends the life span of the patients as well as increases the success rate of local treatments such as surgery and radiotherapy and decreases the toxicity. Although neoadjuvant treatments have no effect on local control, they cause a decrease in radiotherapy-administered volumes. The eradication of micrometastases along with pCR has a prognostic importance.

Nowadays, classical mastectomy is alienated by the options of oncoplastic surgery. The side effects of silicone implants and expanders used, mesh and autologous tissue reconstructions have been enriched with patient images.

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The prognostic factors such as lymph node, grade, tumor volume, histological type, receptor status, Ki 67-index are important in early and local advanced breast cancer. Genetic risk assessment such as HR+ mammaprint, Oncotype DX, PAM-50 Prosigna in early breast cancer determines chemotherapy or hormonotherapy options. The effects and side effect profiles of preferred chemotherapy regimens were compared by meta-analysis and phase III trials conducted by NSABP B-36, Early Breast Cancer Trialists' Collaborative Group and their contribution to life span were discussed. Based on the SOFT and TEXT studies, the alternatives and usage periods of hormotherapy have been updated. In addition to conservative treatments, bisphosphonates recommended by ASCO have also been included in the adjuvant treatment.

Clinical trials like PALOMA-2, MONALEESA-2, MONARCHES-3, and MONALEESA-7 are important guidelines for hormone receptor-positive metastatic breast cancers. The use of CDK4/6 inhibitors in hormone-resistance tumors is an alternative to chemotherapeutics and antiestrogenic agents. In this chapter, phase II–III studies were compared and documented under the corresponding title.

Triple-negative breast cancers account for 15–20% of all breast cancers. The poor prognosis, drug resistance, genetic heterogeneity of triple-negative breast carcinomas and absence of a standard treatment regimen reduce the expected efficacy of chemotherapy. Platinum-based regimens particularly affect the calpain-1 pathway in the endoplasmic reticulum by the DNA damage and apoptosis they cause. This is an important prognostic factor. An increase in the MDA-MB-231 level and a decrease in the MCF-7, BT-474 proteins give a metastatic pattern to the cancer cells. These lead to aggressiveness in the biological characteristics of the tumor and resistance to chemotherapy drugs. In addition to platinum-based treatments, the use of anthracycline and taxanes provides a high rate of pCR, but also causes high recurrence rates during 1–3 year follow-ups. This paradox has still not been clarified. PD-L1, PI3K/AKT/mTOR, histone deacetylase, PARP inhibitors that have recently been brought forward are a few of antiangiogenic treatment options. Antiangiogenic drugs take effect through the angiogenesis induction mechanism of HIF-1 alpha gene. In the study mentioned in this chapter, it was emphasized that the HIF-1 alpha gene would increase the metastasis potential of tumor volume, unlike the subtype of tumor. Therefore, in addition to anthracyclines and taxanes, platinum-based chemotherapies also continue to be relevant.

Liquid biopsies, which have been started to be used in the treatment recently, help detect the tumor cells extravasated into the blood or lymphatic system. The CellSearch™ system helps diagnose by a rate of 20–30% in patients with early breast cancer. It is a leading biomarker in the monitoring of the treatment of the disease.

1.2. Alternative therapies

Dietary bacteria such as polyphenols, genistein, lactospirae, ruminococcaceae, Corynebacterium, staphylococcus, *E. coli*, actinomyces affect the immune system. Chemotherapeutic agents increase toxicity, fatigue, and infections such as cachexia, mucositis, and diarrhea by depressing the immune flora. Supplementing the diet with pre- and probiotic agents with the purpose of reducing the therapeutic effects of drugs shortens the regeneration period of the cells.

Photodynamic treatments and nanomedicine have fewer side effects compared with conventional treatments. They increase the treatment tolerance by affecting the cancer cells in the target tissue. In the future, cancer vaccines, oncolytic virotherapy, immunotherapy options will take a part in the practice a lot more.

2. Palliative approaches

Palliative and psychological support should also be given in the treatment management. Level of education, proximity, and level of love between patient and family, cultural structure of the society and strength of religious values, success of the patient and his/her family in managing the disease process play an important role in the treatment management.

With "Breast cancer and Surgery," a broad perspective was presented to patients with breast cancer in this chapter. Up-to-date information was provided to most clinicians and physicians in the training period. Algorithms to be followed from the diagnosis phase to the treatment and follow-up period of the disease are expressed in a certain manner. I believe that the "IntechOpen" series will be an important reference guide.

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