

Breast Cancer - Past, Present and the Future:

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If anyone thinks he knows all about breast cancer, he probably knows nothing about it. The treatment of no other cancer has been so extensively studied, researched and debated over the last century. The Halsteadian view of a predictable pattern of spread and therefore the most radical loco-regional control (surgery) formed the basis of most of the treatment protocols for the management of this dreaded cancer until late twentieth century. The approach showed gratifying results in the form of reduction in mortality with an expected result, an increase in the morbidity. The living problem being better than a dead solution, it was fairly acceptable at that time as the reduction in mortality was the aim. The treatment of breast cancer continued to be radical and more radical surgery but the survival rates did not show significant improvement after reaching a plateau in the mid twentieth century.

Halstead vs. Fishers view and the middle path:

In the seventies and eighties, the Fishers view changed to a great extent our perception about cancer and it was proposed that breast cancer is a systemic disease at the very inception, therefore a local extra-radical approach recommended by Halstead was not justified, a treatment for the systemic micro-metastases that did not show at the time of first presentation became mandatory. This also explained to an extent the reasons for distant failures inspite of an extra radical treatment locally. Thus came the role of effective adjunctive therapies like chemotherapy and /or radiotherapy along with hormonal therapies.

Fishers view presented a rather depressing scenario as if it was a fight against the inevitable (systemic disease at inception!!). The thought although noble could take away the initiative from the cancer treating clinician. There had to be some truth outside this concept also i.e. probably both local and distant or systemic treatment would be necessary. The role of neoadjuvant chemotherapy for the micrometastases present at the time of initial presentation in most of the breast cancers therefore became important^{1,2}.

The middle path:

While Halstead's view is adapted and based on the predictable pattern of spread of malignancy has become the basis for *sentinel node mapping and biopsy*, systemic neoadjuvant and adjuvant therapies have become an integral part of therapy for breast cancer based on the Fishers view. Thus the middle path [or shall we say the middle path of Buddha!] now forms the basis of treatment for breast cancer.

“The opposite of a correct statement is a false statement, the opposite of a profound truth will be another profound truth”—Niels Bohr

The research in to the molecular biology of breast cancer has enabled us to learn more about the different behavior patterns observed in cancers in two different patients staged and graded

similarly. To a great extent this has also made it possible, to assess the response patterns to various therapeutic regimes^{2,3,4}. In future it should surely be possible to assess and predict the response of breast cancers to a particular therapeutic regime with targeted therapies further helping in getting the optimum response. The tailoring of the treatment protocols for a particular patient would not only improve survival but will also be helpful in avoiding the toxic chemo/radio therapeutic regimes in patients that are likely to be non-responders.

Surgery alone therefore is no longer the only treatment modality for breast cancer. With organ preservation becoming the theme of cancer management, effective adjuvant and adjunctive therapies are also going to play a significant role in the management of breast cancer. In order to, therefore preserve an organ or to perform a less radical and mutilating surgery it is mandatory to have an effective adjunctive therapy available. Further research in to finding out effective markers of response to chemotherapy is therefore required in order to find out the responders and non-responders. In a prospective study the *author* had observed the role of toxicity as a predictor of response to neoadjuvant chemotherapy^{1,2}. This ongoing study has been able to highlight the role of toxicity as a predictor of response to neoadjuvant chemotherapy successfully. When titrated against the apoptotic markers and other biological markers it was found to be a sensitive, effective and cheap solution to predicting response to chemotherapy in a poor country like ours.

Role of surgeon:

The message to be carried home is “it is worthwhile thinking about organ preservation, in this case, breast preservation if the results of the surgery are R0 resection (microscopic freedom from disease)”. However, no amount of chemo and/or radiotherapy is a replacement for a bad i.e. an inadequate surgery. The surgery has to be optimum and surgeon's role continues to be pivotal. The initial diagnosis and initial management are his domain but it is a group of professionals rather than, the surgeon alone, that needs to be involved in the management of breast cancer.

Other therapies

While there has been a tendency to move more and more towards organ preservation with therapies becoming more and more conservative, the adjunctive modalities have assumed greater significance and have developed in to becoming less and less morbid and more focused.

HER-2neu receptor status and chemotherapy:

The newer drugs like Herceptin based on the HER-2 neu receptor status are showing remarkable results in terms of response and survival. Her-2 neu over-expressing tumors show an extremely positive response to trastuzumab (Herceptin), which is a monoclonal IgG, humanised murine antibody directed against extracellular portion of Her-2/neu being used in the treatment of advanced metastatic breast carcinoma. In Her-2 neu positive

tumors trastuzumab therapy is associated with longer time to disease progression, higher rate of objective response, longer, duration of response and longer survival^{5,6}.

Hormone therapy and the aromatase inhibitors:

Breast cancers have traditionally been managed using Tamoxifen, an antiestrogenic drug with endometrial carcinoma and osteoporosis as the most dreaded side effects. First and second line of aromatase inhibitors have also been used and found to improve survival rates. They have been used after Tamoxifen therapy and also as the sole modality with improved survival rates demonstrated in many studies⁵.

Future:

The hope lies in the early diagnosis with effective, widespread National screening programmes and better understanding of the genetics and biological behavior of the disease. Unlike in the western countries our cancers continue to be locally advanced at presentation with very little hope of organ preservation. A dedicated awareness programme is mandatory along with screening facilities if mortality and morbidity from this cancer have to reduce. We in any case must find "Indian solutions to Indian problems". The future therapies are likely to become more and more tailored and targeted with an aim to preserve the form and function without a compromise on the disease survival.

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