

Locally Advanced Breast Cancer: An Enigma!!

Locally advanced breast cancer (LABC) is defined as a non-metastatic advanced breast cancer usually more than 5 cm in diameter and/or characterized by infiltration of skin and/or pectoralis major muscle. Presence of fixed axillary lymph nodes (fixed to each other or axilla) irrespective of the tumor size is included in the locally advanced breast cancers provided there are no detectable metastasis at presentation. According to the AJCC classification LABC includes cancers in the stage II(b) onwards. Any T with N2 M0 disease would also be considered locally advanced.[1-5]

Most patients presenting in the developing countries are locally advanced and their assessment includes a thorough clinical examination and investigations to ascertain operability.[1-3, 6-8] Since the management protocols for LABC have shifted more and more towards multi-modality therapy including neo-adjuvant chemotherapy followed by surgery and /or radiotherapy and hormone therapy, accurate assessment of the initial disease and subsequent serial assessments to measure the response rates become mandatory. The advantages of neo-adjuvant chemotherapy are more or less established and include the down staging of the disease along with management of micro-metastasis that are not detected at the time of initial presentation. The neo-adjuvant chemotherapy also serves as an *in vivo* chemosensitivity test for a particular chemotherapeutic regime and a second line of chemotherapy may be initiated in non-responders for optimum response and minimal toxicity.[1-8]

Since the assessment would be mandatory for the planning of optimum therapy, it can be divided in to the initial assessment i.e. before starting the therapy and subsequent serial assessments as the therapy progresses in the form of neo-adjuvant chemotherapy. The

assessment done initially would be the routine work up for any patient for breast cancer beginning with a detailed history including the family history to arrive at the initial diagnosis and staging. In a LABC further effort would have to be made to exclude metastasis as the management changes drastically for a metastatic breast cancer.

Initial Clinical Assessment

This includes triple assessment in the form of thorough clinical examination followed by imaging (mammography/ultrasound) and fine needle aspiration cytology. The patient is assessed for performance and nutritional status as both significantly affect the out come in these patients.[5] Performance status is assessed by using the Karnowsky scale or ECOG criteria. Local clinical assessment involves a good examination of both breasts starting with the opposite breast first. Examination pattern and the staging for male breast cancer is on the same lines as their female counterparts, it is just that most cancers in males are locally advanced at presentation.

Local Examination

The important aspects of the local examination would include the accurate assessment of the size, fixity to the skin or underlying muscle, presence of *peu de orange* or dimpling. Both axillae and supraclavicular fossae should be examined for presence of lymph nodes and their fixity. Any features like retraction of nipple or puckering need to be mentioned clearly in the initial assessment chart. In a fungating mass these features are obvious and one may have a pictorial record of the findings for subsequent comparison (especially if the patient is put on neo-adjuvant chemotherapy).

Systemic Examination

The systemic clinical assessment would include examination of abdomen for any organomegaly particularly liver and /or presence of ascites to rule out an M1 disease. Examination of spine and chest along with breast is mandatory as these too are common metastatic sites.

P/V and DRE

Per vaginal examination and the digital rectal examinations are mandatory to rule out peritoneal deposits (*Blummer shelf*) or Kruckenberg's tumour (in pre-menopausal women).

Clinical Assessment as a part of Assessing Response to NACT

The serial examinations of the breast and other systems as discussed along with the initial assessment are important to look for any sign of metastasis and also to assess response to therapy that the patient is on. The sensitivity of this examination is poor due to excessive local scarring that may follow the NACT. The response to NACT may be described as complete if the tumour size reduces by more than 50% after three cycles of NACT and those patients with less than 50% reduction in tumour size are taken as non- responders. The clinical assessment may also include use of ultrasound as its natural extension. The ultrasound has often been described as the stethoscope of the surgeon and the sensitivity of the clinical assessment improves with the use of ultrasound significantly [1,2,3,4]. Any appearance of a metastasis during the follow up after neo-adjuvant chemotherapy would make the disease metastatic and change the final management therefore a regular assessment in these patients is mandatory and is a dynamic rather than a static affair. Features of toxicity like alopecia are assessed along with if or not the patient is responding to the chemotherapeutic regime. There are

studies to suggest a correlation between response to neoadjuvant chemotherapy and the toxicity induced i.e. responders have been found to have more toxicity.[5]

Summary

The clinical assessment is a dynamic process and is done before the initiation of therapy and subsequently continues serially to assess the response and the appearance of a metastasis. The appearance of the metastasis changes the stage and the management of the patient. Thorough history and clinical examination forms the basis of subsequent assessment of tumor behaviour and response to NACT which is a routine protocol in the multimodality therapy for the management of locally advanced breast cancer. Use of ultrasound for accurate assessment of size of the tumour as well as presence of axillary lymph nodes.

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References

1. Chintamani, Rohan Khandelwal, Aliza Mittal, S Sai, Tuteja A, Bhatnagar D, Saxena S. Qualitative and quantitative dermatoglyphic traits in patients with breast cancer. *BMC Cancer*. 2007; 7: 44.
2. Chintamani, Binita P Jha, Vimal Bhandari, Anju Bansal, Saxena S, Bhatnagar D. The expression of mismatched repair genes and their correlation

- with clinicopathological parameters and response to neoadjuvant chemotherapy in breast cancer. *International Seminars in Surgical Oncology*. 2007; 4: 5.
3. Chintamani, Singh JP, Mittal MK, Saxena S, Bansal A, Bhatia A, Kulshreshtha P. Role of p-glycoprotein expression in predicting response to neoadjuvant chemotherapy in breast cancer — a prospective clinical study. *World J Surg Oncol*. 2005; 3: 61.
 4. Chintamani, Singhal V, Singh J, Bansal A, Saxena S. Half versus full vacuum suction drainage after modified radical mastectomy for breast cancer - a prospective randomized clinical trial [ISRCTN24484328]. *BMC Cancer*. 2005; 5(1):11.
 5. Chintamani, Singhal V, Singh JP, Lyall A, Saxena S, Bansal A. Is drug-induced toxicity a good predictor of response to neo-adjuvant chemotherapy in patients with breast cancer? — a prospective clinical study. *BMC Cancer*. 2004; 4: 48.
 6. Chakroborty A, Murthy NS, Chintamani, Bhatnagar D, Mohil RS, Sharma PC, Saxena S. CYP17 gene polymorphism and its association with high-risk north Indian breast cancer patients. *J Hum Genet*. 2007; 52(2): 159-65.
 7. Chintamani, Saxena S, Chakroborty A, Agarwal AK, Sharma VK, Sharma PC, Lenoir G, Goldgar DE, Szabo CI. Contribution of germline BRCA1 and BRCA2 sequence alterations to breast cancer in Northern India. *BMC Med Genet*. 2006; 7: 75.
 8. Chintamani, Saxena S, Rekhi B, Bansal A, Bagga A, Murthy NS. Clinico-morphological patterns of breast cancer including family history in a New Delhi hospital, India — a cross-sectional study. *World J Surg Oncol*. 2005; 3: 67.