www.jmscr.igmpublication.org
Impact Factor 5.84
Index Copernicus Value: 83.27
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v5i5.116

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Research Article

Breast Conservation Surgery after Neoadjuvant Chemotherapy in Responders in Operable Breast Carcinoma: A Better Alternative

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Abstract
Background: *This was follow up of twenty five female patients of operable breast cancer in a prospective study in a tertiary care centre over a period of one year from 1st September,2006 to 31st August,2007 regarding response to neoadjuvant chemotherapy and conversion of modified radical mastectomy to breast conservation surgery.*
Aim: *To observe the events during years of follow up and to study whether breast conservation surgery in carefully selected responders could prove to be a better alternative.*
Material and Methods: *The study was conducted in fine needle aspiration cytology proven operable breast cancer patients with ductal histology. Inclusion criteria were female patients with complete haemogram, liver function tests, renal function tests within normal limits, Karnofsky score more than fifty and age below 70 years. Exclusion criteria were patients with pregnancy or previous history of thoracic irradiation.*
Results: *16 of 25 patients were offered breast conservation surgery after neoadjuvant chemotherapy according to selection criteria and kept on follow up after treatment completion. Two patients developed ipsilateral breast recurrence at four and six years of follow up respectively.*
Conclusion: *Breast conservation surgery seems to be a safe and better alternative in carefully selected responders.*
Keywords: *Neoadjuvant chemotherapy ,Breast conservation surgery, Modified radical mastectomy*
Abbreviation: *BCS; Breast conservation surgery, MRM; Modified radical mastectomy, IBTR; Ipsilateral breast tumour recurrence.*

Introduction

Breast cancer has been showing rising trend in India for last two decades.[1] Due to changing life style younger women are suffering from this disease. The treatment strategy has changed from a primarily surgical approach to multimodality treatment. There has been a shift towards less radical surgery. In favourable responders modified radical mastectomy is a serious disservice especially in younger women when a less

mutilating and more cosmetic surgery may be offered. This may prove to be a less traumatic experience physically and psychologically and may help the patients recover fast and have a better self image.

Materials and Methods

The study included 25 female FNAC proved T1-T3, No-N1, M0 breast cancer patients who reported in the department during one year w.e.f. 1.09.06 to31.08.07. General prerequisites for inclusion in the study were Hb>10 gm% , TLC > 4000, Platelet count > 100000, renal and liver function tests within normal limits, Karnofsky performance status >50 and age below 70 years. Patients who had breast cancer along with pregnancy and the patients who did not match the above inclusion criteria were not included in the study. Patients were evaluated by thorough clinical history and detailed clinical examination. Mammography of bilateral breasts and ultrasound of the diseased breast was carried out. The tumour size was measu-red clinically and ultrasonographically before administration of first cycle and clinically before administration of each subsequent cycle. The tumour size was finally assessed both clinically and ultrasonographically two weeks after completion of last cycle of neoadjuvant chemotherapy. The product of two greatest perpendicular diameters was used to quantify the size of the tumour. Two to four cycles of CAF based neoadjuvant chemotherapy were administered to all the patients three weeks apart on day one only as per schedule each time ensuring proper hydration and by giving antiemetics and symptomatic treatment. Neoadjuvant chemotherapy was administered as under:

Inj. Cyclophosphamide 600 mg/m2 I/V infusion on day 1

Inj. Doxorubicin 50 mg/m2 I/V bolus on day 1

Inj. 5-Flurouracil 600mg/m2 I/V infusion on day 1

During treatment patients were monitored for toxicity and response to neoadjuvant chemotherapy.

In the absence of clinical evidence of tumour in the breast, the response to therapy was categorised as clinically complete response (cCR). When the clinical size of the tumour decreased by 50 % or more, the response was judged to be partial (cPR). When there was an increase of more than 50 % in the original size of the tumour after a minimum of two cycles of neoadjuvant chemotherapy, the patient was considered to have progressive disease (cP). Patients whose response criteria did not meet the definitions of either cCR, cPR or cP were considered to have clinically stable disease.

Depending upon the response to neoadjuvant chemotherapy, appropriate surgery was performed in each case, which was either breast conservation surgery (BCS) or modified radical mastectomy (MRM).

The former was either in the form of quadrentectomy or wide local excision combined with axillary dissection through a separate incision. Modified radical mastectomy was performed in those patients who were not fit for breast conservation surgery or had clinically progressive (cP) or clinically stable disease (cS) disease after at least 2 cycles of neoadjuvant chemotherapy.

Patients who had large tumour in a small breast, tumour size more than 4 cm in largest dimension, multicentric disease, were not taken for breast conservation surgery.

The breast conservation surgery or modified radical mastectomy were carried out under general anaesthesia. The palpable lesions were localised sonographically before surgery and non palpable lesions were localised prior to surgery by insertion of a hook wire under ultrasound guidance. An appropriate sized skin incision was made and deepened and dissection was continued towards wire. The specimen having been excised was

immediately oriented before submitting to detailed histopathological examination using sutures. In this study, one suture for anterior margin, two for medial margin and three for inferior margin were used.

Histopathological examination of the surgically removed specimens was done for resection margins and for axillary lymph nodes . In patients showing clinically complete response (cCR), histopathological examination was done to know the extent of pathological response (pCR or pinv.)

Radiotherapy was delivered to intact breasts after breast conservation surgery as:

50 Gray /5 weeks in 25 fractions by tangential portals by Cobalt-60 teletherapy ± boost of 10 Gray /5 fraction covering tumour bed. Radiotherapy was delivered to chest wall and draining area after modified radical mastectomy.

Postoperative chemotherapy was delivered as 4 cycles of CAF based adjuvant chemotherapy 3 weeks apart in all cases . Patients who had clinically stable (cS) or clinically progressive (cP) disease after neoadjuvant chemotherapy were administered taxane group of drugs.

Results

One patient was in 21-30 years age group while 5 in 31-40, 10 in 41-50 and 9 in 51-60 years age group. 11 patients were premenopausal and 14 postmenopausal.

19 patients were T3N1M0, 1T3N0M0, 1 T2N0M0 and 4 T2N0M0 before delivering neoadjuvant chemotherapy and 12 patients were staged T2N1M0 after neoadjuvant chemotherapy, 8 T2N0M0 and 1 patient each T3N0M0, T3N1M0.

Neoadjuvant chemotherapy reduced the tumour size substantially. Response was noted in 84% patients, clinically partial response in 72% and clinically complete response in 12%. Tumour to breast ratio was found adequate in 22 patients. Nine patients could not be offered breast conservation surgery due to various reasons like inadequate tumour to breast ratio, size more than 4 cm in largest dimension, multicentric disease, clinically stable disease and clinically progressive disease.

Ultrasonographically measured size of the tumour was smaller as compared to the clinically measured size both before and after delivering neoadjuvant chemotherapy.

16 patients were considered eligible for breast conservation surgery after neoadjuvant chemotherapy according to selection criteria and were offered the same while pre-chemotherapy only 3 patients were found eligible. Three patients had achieved clinically complete response (cCR) after neoadjuvant chemotherapy and were found to have achieved pathologically complete response (pCR) after breast conservation surgery .None of the patients had positive margins. Patients were kept on follow up after completion of treatment .The median follow up time was 10 years .One patient developed IBTR at four years and the other at six years of follow up .These were in near vicinity of the primary tumour. 6 of 25 patients developed distant metastasis at different intervals of time during follow up, 2 of these were the patients who had developed IBTR earlier.

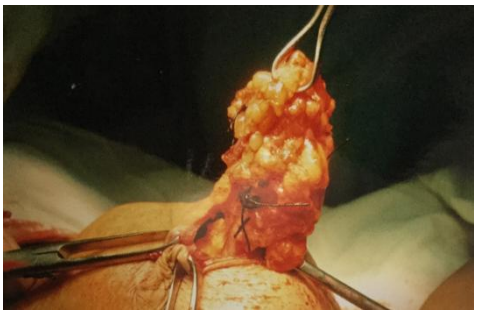

Fig.1 : BCS in progress

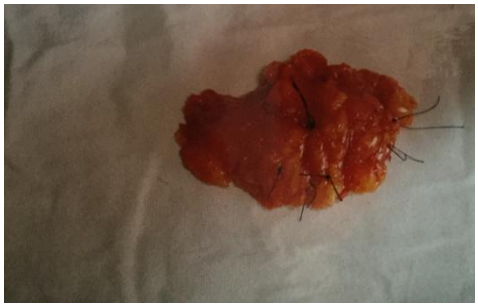

Fig.2 : The oriented specimen

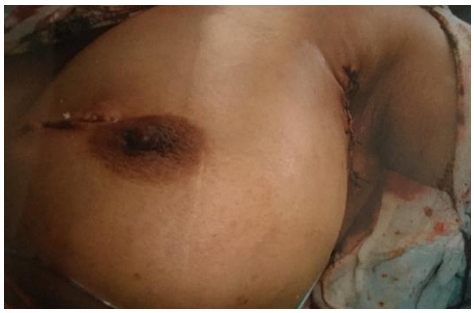

Fig 3 : BCS in upper inner quadrant tumour breast completed

Discussion

Breast conservation surgery rate increases after neoadjuvant chemotherapy in responders. This has been reported in various studies though % increase may differ.[2,3,4,5,6]. In our study, before giving neoadjuvant chemotherapy only three [12%] patients were found eligible for breast conservation surgery, whereas sixteen [16%] were offered this surgery afterwards. The % increase was 52. All patients who were eligible according to selection criteria were offered breast conservation surgery. Some of the patients were totally ignorant about the treatment offered and were ready for any surgery while some others felt that breast removal was the ideal treatment as they had gathered this information through various sources and were apprehensive that breast conservation surgery would leave the cancer behind. Such patients had to be counselled about the outcome of the surgery and were assured that in case of any such happening they always had the choice of modified radical mastectomy. Most of the surgeons were also not forthcoming as they were not sure of the recurrence potential and felt that this may put their reputation at stake. So Majority of the breast conservation surgeries were carried out by a single surgeon who was keen to do this surgery and have an idea of its outcome in our setup. This made the work more convenient, coordinated and oriented.

The surgeon did breast conservation surgeries with an adequate margin that was 1 cm, keeping cosmesis in view at the same time. Significantly less tissue had to be resected after neoadjuvant chemotherapy as the resection was done as if the tumour was smaller initially.[7,8]

On completion of the treatment patients were kept on follow up and the events recorded. There were two ipsilateral breast tumour recurrence, one at four and the other at six years of follow up. This makes it 6.25% at 5 years and 12.50% till date. This is comparable to some large and smaller studies.[9,10,11] There were six [24%] cases of distant metastasis in whole cohort of 25 patients [11,12] of which two were the patients who had developed IBTR that is considered a strong predictor of distant metastasis.[11] The ipsilateral breast tumour recurrence rate is higher with positive margins[13,14] and authors did not have any patients with positive margins. The patients who had achieved clinically complete response (cCR) and pathologically complete response (pCR) subsequently after breast conservation surgery were event free till date.[12] This underscores the influence of pathologically complete response on prognosis of disease .

11 patients were premenopasal and 14 were postmenopausal in this study that makes the distribution approximately at par though it is said to be presented more in postmenopausal women.

16 patients presented in 3rdto 5th decade of life , only 1 in 3rd while 15 in 4th to 5th decade, 10 of these in 5thdecade closely followed by 9 patients in 6thdecade as is the presentation in India where majority of the patients present in 4th to 6th decade of life.[1]

As patients are more likely to turn up as responders in younger age groups, these being hormone receptor negative and chemotherapy sensitive.[15] So may prove to be the best beneficiaries but authors could not observe any such correlation probably due to small no. of cases and influence of factors like molecular subtype or tumour biology. 4 non responders were found. 1 in 4th, 2 in 5thand 1 in 6th decade of life.

The tumour size was large at presentation in majority of cases that shrank to a size to allow breast conservation surgery. Most of the patients were not candidates for breast conservation

initially. As response was a major criteria to select patients for breast conservation surgery, maximum no. of patients who could be allowed were taken for the surgery. The apprehension that recurrence rate may turn up to be high did not prove to be true as in the neoadjuvant setting prognosis depends upon response to therapy.[15]

The influence of residual disease after neoadjuvant chemotherapy on prognosis was seen as the patients with large tumours whose tumours had shrunken considerably and N1 axillary lymph nodes had turned N0 were event free till date .This suggests that chemosensitivity and responsiveness of disease influences prognosis.[15]

The authors used mammography and ultrasonography as imaging studies and size of the tumour was found to be smaller to the clinically measured size due to desmoplastic reaction.[16,17] that may be the reason for negative margins. The IBTR were found in cases where tumour size was large initially and had responded partially to fall under purview of breast conservation surgery.[14]

As selection criteria for breast conservation surgery improve with better imaging modalities like magnetic resonance imaging that can predict patchy cytoreduction as well as pathologically complete response[18], though known to overestimate the residual disease , there will be less risk of recurrence and more acceptance by patients as well as surgeons and more patients may be offered this surgery .

Conclusion

Use of neoadjuvant chemotherapy is common approach in stage II and III operable breast cancer [19] and the authors found that with proper selection criteria and multidisciplinary coordination excellent local control rates could be achieved in responders who otherwise were candidates for MRM .[20]

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