



Post Neo Adjuvant Chemotherapy(NACT) changes in Breast Carcinoma

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ABSTRACT

Neoadjuvant chemotherapy(NACT) is given in the pre operative period for earlier stage operable cases.Our study is focused on the pathologic changes in breast cancers after Neoadjuvant chemotherapy,to assess residual tumor burden,to follow recommendations for pathologic examination and reporting and comparing clinical and pathological response to chemotherapy.

KEYWORDS : NAT,residual cancer burden,pathologic response

INTRODUCTION

Neoadjuvant chemotherapy is the standard of care for the treatment of locally advanced breast cancer.Its benefits are limited operation, such as lumpectomy, instead of mastectomy and the potential response of the tumor to further treatment.

MATERIALS AND METHODS

The present study is a prospective study of 12 patients in 3 months period taken 2 to 6 cycles of Cyclophosphamide 50 to 60 mg/m² iv & Doxorubicin40 to 50 mg/m² iv. Clinical and pathologic response to chemotherapy was assessed

Data collected includes histologic diagnosis on pre-treatment core biopsy,tumor and axillary lymph node status both clinically & radiologically,length of chemotherapy and the drugs used,size and location of the tumor,clinical and radiologic impression of treatment response,tumor size,cellularity,histologic appearance and tumor grade and response in lymph nodes are assessed.

Systems used for Reporting (Table1)

TABLE - 1

Criteria Used in Different Systems for Categorizing Response to Treatment ¹
<p>NSABP B-18 Category pCR No recognizable invasive tumor cells present pPR The presence of scattered individual or small clusters of tumor cells in a desmoplastic or hyaline stroma pNR Tumors not exhibiting the changes listed above</p>
<p>Miller-Payne System² Grade 1 No change or some alteration to individual malignant cells, but no reduction in overall cellularity (pNR) Grade 2 A minor loss of tumor cells, but overall cellularity still high; up to 30% loss (pPR) Grade 3 Between an estimated 30% and 90% reduction in tumor cells (pPR) Grade 4 A marked disappearance of tumor cells such that only small clusters or widely dispersed individual cells remain; 90% loss of tumor cells (almost pCR) Grade 5 No malignant cells identifiable in sections from the site of the tumor; only vascular fibroelastotic stroma remains, often containing macrophages; however, ductal carcinoma in situ may be present (pCR)</p>
<p>RCB System³ RCB-0 No carcinoma in breast or lymph node (pCR)</p>

RCB-I Partial response RCB-II Partial response
RCB-III Chemoresistant

AJCC "y" Classification

Category

T Uses same criteria as before treatment

N Uses same criteria as before treatment

* NSABP indicates National Surgical Adjuvant Breast and Bowel Project; pCR, pathologic complete response; pPR, pathologic partial response; pNR, pathologic no response; DCIS, ductal carcinoma in situ; RCB, residual cancer burden; and AJCC, American Joint Committee on Cancer.

Reporting of breast carcinomas after NACT:

Breast specimen

1. Presence and size of tumor bed
2. Size and extent of residual tumor
3. Average cancer cellularity of residual tumor bed
4. Appearance of residual tumor and grade
5. Viability(necrosis, mitotic figures)
6. Lymphovascular invasion
7. Presence and extent of DCIS
8. Margins with respect to tumor bed
9. Comment on overall response to treatment

Lymph nodes

1. Number of lymph nodes
2. Number of lymph nodes with metastases
3. Size of largest metastases
4. Presence of extra nodal extension
5. Number of metastases with evidence of treatment response
6. Number of metastases with evidence of treatment response but without tumor cells.

RESULTS

Median age is 45 years,mean size of tumor before chemotherapy - 15.2 cm²,after chemotherapy -10.3cm² and reduction in mean tumor size by 32%. There is consistent decrease in size.

Histological findings were divided as pathologic changes in tumor cells and changes in the stroma.

Changes in Tumor cells include loss of architecture,dyscohesion ,shrinkage of tumor cells with retrogressive changes like karyorrhexis, karyolysis, pyknosis .Viable tumor cells were seen having distinct nuclear chromatin with intact nuclear and cytoplasmic membrane and absence of criteria of necrosis.

(Figure:1,2)

Changes in stroma included elastosis/ collagenization, hyalinization of the walls of the bloodvessels ,atrophy of adjacent breast parenchyma and cancerization of ducts even in atrophic lobules.Other changes include stromal fibrinoid necrosis and mucinous change.(Figure:3)

Inflammatory host response was seen in the form of lymphocytic/ mixed /plasmacytic or prominent histiocytic and giant cell type) (Figure:4)

Figure 1:Chemotherapy changes in tumor tissue(Bi 4997/15,H&E 10x)

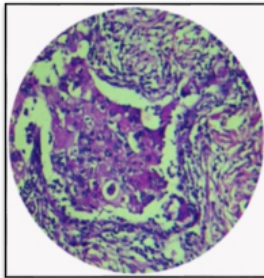


Figure 2:Chemotherapy changes in tumor tissue

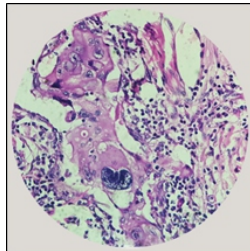


Figure 3:Stromal response(Bi 1250/16,H&E 40x)

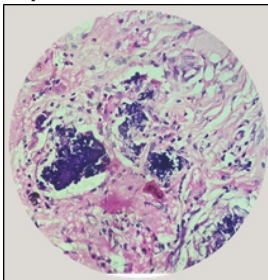
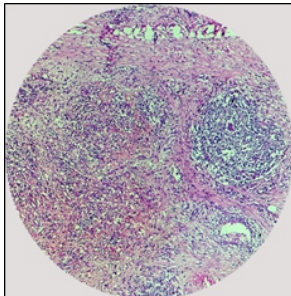


Figure 4:Stromal inflammation



DISCUSSION

Comparison of size of the tumor(product of two largest orthogonal diameters)before and after neoadjuvant chemotherapy revealed reduction in size of tumor.

Clinical assessment showed complete response in 25% cases,partial response in 66.66% and stable disease in 8.33% cases.

After NACT, no patient progressed during the treatment with chemotherapy

Histologic assessment showed nil complete pathologic

response.Partial response seen in 91.7% and stable disease in 8.33% caases.(Table-2,3)

Results were compared with other studies.(Table-4)

TABLE-2

Correlation of stromal response seen after NACT and pathologic response grades

Stromal host response	No. of cases (%)	Complete response	Partial response(%)	Stable disease(%)	Progressive disease
Elastosis/collagenization	100	0	91.66	8.33	0
Microcalcification	16.6	0	100	0	0
Stromal fibrinoid necrosis	100	0	91.66	8.33	0
Hyalinization of vessels	100	0	91.66	8.33	0
Mucinous change	8.33	0	100	0	0

TABLE-3

Correlation of inflammatory response seen after NACT and pathologic response grades

Inflammatory host response	No. of cases (%)	Complete response	Partial response	Stable disease	Progressive disease
Mixed	2	0	2	0	0
Lymphocytic grade 1	5	0	4	1	0
Lymphocytic grade 2	3	0	3	0	0
Lymphocytic grade 3	1	0	1	0	0
Plasmacytic	0	0	0	0	0
Prominent histiocytic	0	0	0	0	0
Giant cell type	1	0	1	0	0

TABLE-4

Carcinoma breast - comparison of complete clinical and pathologic response

	Complete clinical response (%)	Complete pathologic response (%)
Swain <i>et al.</i>	49	62
Vander wall <i>et al</i>	20	5
Cameron <i>et al</i>	5	10
Sorace <i>et al</i>	50	70
Moon <i>et al</i>	26	8
Chevallier <i>et al</i>	29	26
Demaria <i>et al</i>	24	4
Present study	25	0

CONCLUSION

Regarding the response to chemotherapy many fallacies exist in evaluating the clinical response,so pathological evaluation is the gold standard.

Pathologists play an important role in providing the information regarding approach to therapy and is vital in standardizing the classification.

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