

Histo-Pathological Evaluation of Breast Cancer after Neo-Adjuvant Chemotherapy

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ABSTRACT

Background: A recent standardized therapeutic technique for the patients having advanced and large (bigger than two centimeters) breast cancer is neo-adjuvant chemotherapy. The gold standard is the histo-pathological assessment of carcinoma response.

Methodology: In this research study, we performed the histo-pathologic evaluation of forty-four samples received in the pathology department over a period of one year from 1 July 2021 to 30 June 2022.

Results: In this research study, we studied total forty-four patients with breast cancer. Average age of these females was fifty years. Average size prior CT was 56.140 centimeter square and post CT was 29.4 centimeter square. In this research work, complete pathologic response was shown by eighteen percent patients and incomplete response was shown by eighty-four percent patients.

Conclusion: Changes in pattern of characterizations examined after the histo-pathological evaluation of tumor are dystrophic calcification, stromal hyalinization, regions of coagulated necrosis, reactive infiltration of lymphocytes, cellular fibrous tissue and hemosiderin laden macrophages.

Keywords: Characterization, pathology, evaluation, neo-adjuvant chemotherapy, carcinoma, cancer, average.

INTRODUCTION

Neo-adjuvant chemotherapy is recently recognized as standard therapeutic technique for the patients having advanced and larger than two center breast tumor [1]. There is no establishment of the ideal instructions for pathologic assessment of breast samples after NAT (2-7). Evaluation of the measurement of residual complication in site of breast or/ and lymph node and therapeutic response are much vital because these assessments may forecast survival and gives instructions for future treatment [7, 8]. This current research study will discuss field of histologic changes that can be observed in malignant tissues of breast and also determine how to assess, take specimen and measure the residual breast carcinoma in excised samples together with axillary lymph nodes after application of neo-adjuvant chemotherapy.

Breast cancer is the most frequently occurring cancer among women in the developed as well as developing countries and it has become the major public health problem worldwide with nearly 1.7 million newly diagnosed cases in 2012 representing 25% of all female cancers. Among Nepalese women, breast cancer is the second most common type of cancer accounting 6% of total cancers in Nepal. In Nepal, more than one quarter of the breast cancer is diagnosed in young female and many being diagnosed at an advanced stage with tumors showing more aggressive biological behaviors. The familial history of breast cancer and mutation of tumor suppressor genes BRCA1, BRCA2 and p53 increases risk of breast cancer. Alcohol consumption, high dietary fat intake, obesity, overweight, diabetes mellitus and physical inactivity has induced breast cancer incidence. Breast cancer is commonly diagnosed in female with late menarche, early pregnancy, long lactation period, less breast feeding, change in lifestyle and dietary habits, familial history of breast cancer and contraceptive users. The histopathological factors of breast tumors like tumor size, lymph node status, histological type, histological grade, presence or absence of hormone receptors and age of patients play crucial role on chemotherapy and radiation therapy. The study aims to assess the clinical profile of the patients with breast carcinoma as well as macroscopic and microscopic features of MRM specimens. Histopathologic assessment of breast cancer has long provided the basis for prediction of recurrence risk and prescription of adjuvant therapy. The features routinely documented include tumour size, type, grade and the presence of axillary lymph node (LN) metastases. In addition, presence of

estrogen and progesterone receptors (ER α and PR) is assessed principally to indicate the potential value of endocrine therapy. Recently, gene expression studies, which combine data on expression of thousands of genes with powerful computational analysis, have given new insight into breast cancer biology. In particular, these studies have demonstrated that subtypes of breast cancer with a predictable clinical course can be defined and reproducibly identified on the basis of gene expression patterns. In this is a compelling demonstration that tumour biology has a pervasive impact on clinical outcome. Furthermore, evidence that the essential biological character of breast cancer is apparent early in disease development comes from the detection of the same discriminant gene expression profiles in early-stage breast cancer, more advanced lesions and metastases.

In common with global gene expression patterns, the histopathologic features of breast cancer reflect the influence of a number of biological processes including not only those operating in cancer cells but also cancer-stromal interactions and complex immune and hormonal influences. However, in addition to biology, the histopathology 'snapshot' of a cancer incorporates the period of opportunity that morphological features have had to develop. In the light of recent revelations on the natural history and clinical importance of breast cancer biology, it is timely to consider how biology is reflected in histopathologic parameters. Population mammographic screening, effecting preclinical detection and regular re-examination, provides an opportunity to examine the relative contribution of biology and time to development of the major histopathologic features of breast cancer. We have examined this issue in a large cohort of screen detected breast cancers that were subject to central histopathology review. Pathologic features of breast cancer diagnosed at a first screening round (prevalent) were compared with incident cases on the basis that prevalent cancers have potentially longer to develop prior to detection than incident cancers where this is theoretically limited by screening interval. In addition, for incident invasive breast cancers, histopathologic features were compared with the interval between the diagnostic screening round and the previous negative screen.

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breast samples after NAT (2-7). Evaluation of the measurement of residual complication in site of breast or/ and lymph node and therapeutic response are much vital because these assessments may forecast survival and gives instructions for future treatment [7, 8]. This current research study will discuss field of histologic changes that can be observed in malignant tissues of breast and also determine how to assess, take specimen and measure the residual breast carcinoma in excised samples together with axillary lymph nodes after application of neo-adjuvant chemotherapy.

Aim: The aim is to investigate the spectrum of histo-pathological results of breast cancers after application of neo-adjuvant chemotherapy.

Objectives: To investigate the total and microscopic alterations made after NAT in influenced breasts.

To examine the pathologic reaction to applied therapy

METHODOLOGY

This is a prospective research work in which total forty-four patients were recruited from MRM specimen of post chemotherapy obtained in the Pathology Department of Mayo Hospital, Lahore, Pakistan over a period of complete one year from 1 July 2021 to 30 June 2022. In this study, paclitaxel based chemotherapy was given to patients for four to six cycles (Adriamycin, Cyclophosphamide & paclitaxel) and all these patients underwent improved radical mastectomy with dissection of axillary lymph node. We used a well-organized form for recording the past history of the patients with gender, age, profession, duration of the complication, residence area, past history of surgical intervention, radiotherapy and chemotherapy. We fixed the tissue obtained for histo-pathological assessment in 10.0% formalin. After suitable fixation, samples underwent complete gross investigation. We took the multiple bits from obtained tissue after suitable designation of margins and gross examination. We also evaluated the background tissues at many points and resection of the available lymph nodes and submitted for further processing to check the further spread of tissue. We used the automated tissue processor for the processing of tissues. We made the Paraffin blocks and used microtome to cut the five to six sections of microns. We stained the slides with H & E (Harris Hematoxyline & Eosin stain).

We studied the post-chemotherapeutic alterations from the specimens of MRM. We performed the histological grading with the utilization of grade system of Bloom Richardson. The grading of the histo-pathological evidences of the chemo-therapeutic response was carried out from the sections of H & E. We defined the complete pathological response as complete tumor's disappearance from breasts without any negative lymph nodes and invasive carcinoma.

RESULTS

We included total forty-four patients having range of age from twenty-one to seventy years. Average age of the patients was fifty years. All the participants of this research work were from female gender. Fifty-five percent females were pre-menopausal and forty-five percent females were post-menopausal. All the participants obtained regimen of CEF drug for chemotherapy. Most of the patients (35.0%) obtained six chemotherapy cycles followed by four chemotherapy cycles (11.40%). All the females were present with unilateral lump of breast. The most common site was center quadrant (38.630%) followed by 22.720% upper inner quadrant. There was presence of most of patients with fixed breast abrasion (95.50%).

Average size before CT was 56.140 centimeter square and post CT was 29.400 centimeter square. We found the significant decreased size after the chemotherapy in comparison with size prior to chemotherapy (P-value < 0.00010). We noted the significant difference after application of chemotherapy showing noteworthy conversion of hard and firm abrasions to fleshy abrasions. (Pearson Chi square value 5.5000 a, continuity correction b-value 3.8190, Likelihood ratio -6.0670).

Among total forty-four patients, we diagnosed 79.50% patients with IDC followed by 6.80% patients with suspicion of malignancy, 4.50% patients with adenocarcinoma, 2.30% patients with DCIS, 2.30% patients with ILC, 2.30% patients with metastatic adenocarcinoma and 2.30% patients with infiltrating carcinoma prior chemotherapy. Most of the patients about 75.0% recognized with IDC followed by 15.90% patients without residual tumor, 6.80% patients with DCIS, 2.27% patients with adenocarcinoma after the application of chemotherapy [7]. Total 15.90% patients were presented without any malignant cell after sampling of extended level.

In 9.09% (N: 04) patients, there was presence of microscopic foci of tumor cellular bodies, 9.09% (N: 04) patients were present with microscopic diffuse carcinoma. There was no visibility of the macroscopic tumor but at histologic investigation, we noted down the tumors cells diffuse infiltration. Macroscopic tumor was present in 65.90% (N: 29) patients. Margins of most of the cases (84.1%) were tumor free. Among total forty four patients, forty two patients (95.50%) displayed fibrosis, 81.80% (N: 36) patients shows necrosis, 97.70% (N: 43) patients shows chronic cell infiltration inflammation, DCIS component was present in seven patients (15.90%), 27.30% (N: 12) patients were available with vascular invasion, 20.50% (N: 9) patients displayed lymphatic invasion, 13.60% (N: 6) were with calcification and 47.70% (N: 21) patients underwent hemorrhage. Most common alteration examined is inflammatory host response. Lymphocytic is the most common inflammatory host response comprised plasmacytic, histiocytic and mixed inflammation type.

Table-1 is describing the tumor's characteristics after application of chemotherapy. The response of 15.90% (N: 7) patients was complete without any malignant cell as detected during sampling of extended level. Total 9.09% (N: 4) patients were present with microscopic foci and four patients were present with microscopic diffuse carcinoma. Table-2 displays the abrasions after application of chemotherapy.

Table 1: Tumor's characteristics after CT

Tumor's characteristics	Repetition	Percent (%)
No remains	7.0	15.90
Marginal microscopic	4.0	9.1
Diffused microscopic	4.0	9.1
Macroscopic remains	29.0	65.90

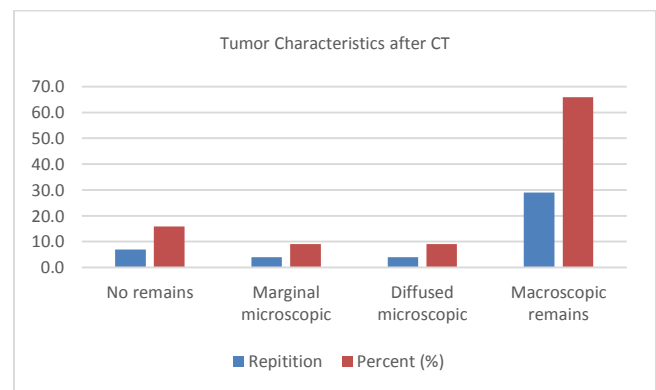
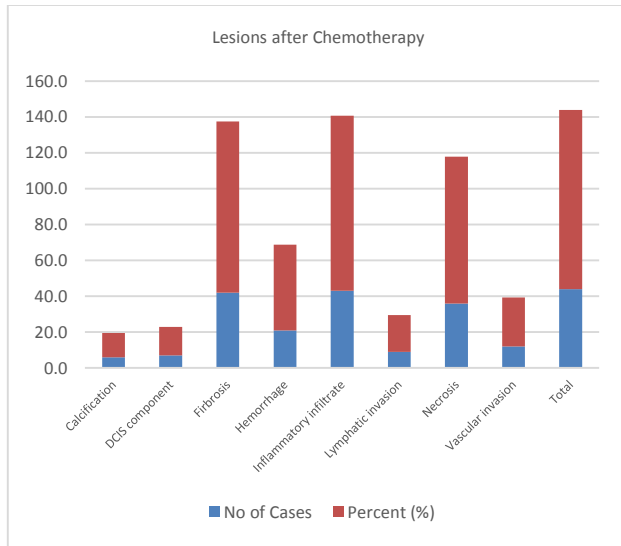


Table 2: Lesion's characteristics after CT

Characteristics of lesion	No of Cases	Percent (%)
Calcification	6.0	13.60
DCIS component	7.0	15.90
Fibrosis	42.0	95.50
Hemorrhage	21.0	47.70
Inflammatory infiltrate	43.0	97.70
Lymphatic invasion	9.0	20.50
Necrosis	36.0	81.80
Vascular invasion	12.0	27.30
Total	44.0	100



DISCUSSION

Pathologist’s role is to evaluate effect of chemotherapy on breast cancer. In this current research work, the range of the age of the patients was twenty one to seventy years in which peak age group was forty one to fifty years of age organizing 36.0% patients. Average age of the patients for abrasion’s presentation was fifty years which is consistent with the findings of other research works [9, 10] displaying the average ages as 50.60 and 48.90 years correspondingly. All the participants of this research work were females, which is similar to many other research studies [10, 11, 12, 13]. In current research work, among forty-four patients, 55.0% (N: 24) females are pre-menopausal and 45.0% (N: 20) females are post-menopausal which is consistent with one other research study [14]. One research study reported the highest amount of the pre-menopausal females 77.0% (N: 734) [15].

In current research, 75.0% (N: 33) patients were stated as IDC, three patients stated with DCIS and one patient was present with adenocarcinoma after application of chemotherapy whereas seven patients gave complete response no malignant cells after sampling of extended nature. One other research work [13] stated 79.20% patients as IDC, 2.10% female patients as ILC. One research study [15] stated 76.0% patients as IDC, seven percent patients as ILC and three percent patients were other cases. Other research study [16] described ninety-six percent patients as IDC and four percent patients as ILC. One other study [17] stated ninety-four percent patients as IDC and two percent patients with other cases. Narendra in 2018 stated ninety-six percent patients as IDC and four percent patients as ILC [14].

In this current research study, eighteen percent patients showed complete response to pathology and eighty-four percent patients were available without complete response. The incomplete response was because of advance stage of the complication. Hamy-Petit in his study conducted in 2016 [17], stated the thirty-nine percent patients with complete response to pathology and 60.90% patients were available with incomplete pathologic response. Jung YY [18] stated 46.20 percent patients with complete response to pathology and 53.80% patients without complete response. One other study stated 27.10% patients with complete and 72.90% patients with incomplete pathologic response [13]. In one other research study, 83.63 percent patients were having incomplete and 9.0% patients were present with complete response to pathology.

The results of this current study are similar with the findings of many other researches. Ramana Kumari stated the changes in the spectrum of tumor bed are bizarre nuclei, necrosis, hyalinization, intense mono-nuclear collection of inflammatory cells

and cytoplasmic vacuolization [12]. Chakrabarti also examined frequent morphological alterations in histological assessment were reduced cellularity, inflammatory cells bodies as 61.50%, fibrosis as 64.10% and necrosis as 30.80% [19, 20].

CONCLUSION

The findings of this research work concluded that histo-pathological evaluation of tumor bed is ideal standard for examining chemo-therapeutic response of tumor. Changes in pattern of characterizations examined after the histo-pathological evaluation of tumor are dystrophic calcification, stromal hyalinization, regions of coagulated necrosis, reactive infiltration of lymphocytes, cellular fibrous tissue and hemosiderin laden macrophages.

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