

CASE REPORT

PATHOLOGY OF BREAST CARCINOMA AFTER NEOADJUVANT CHEMOTHERAPY: A CASE REPORT WITH REVIEW OF LITERATURE

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ABSTRACT: Accurate pathological diagnosis of tumor mass before treatment and careful examination of specimen after the treatment are the two main objectives in the diagnostic process of neo-adjuvant retreated breast carcinomas.

KEYWORDS: Neo adjuvant chemotherapy, Carcinoma breast, Infiltrating duct cell carcinoma.

INTRODUCTION: Neo adjuvant chemotherapy has been used for a primary treatment for inoperable locally advanced or inflammatory carcinomas, but recently it is extended to operable breast carcinomas also.⁽¹⁾ The aim is to evaluate the tumor response to neo adjuvant chemotherapy in breast carcinomas.

CASE REPORT: A female patient observed a lump in left breast since 1 year back and on F.N.A.C. duct cell carcinoma was diagnosed. She received 6 cycles of Neo adjuvant therapy (NAT) and she underwent modified radical mastectomy with axillary lymph nodal dissection.

Before neo adjuvant chemotherapy, on clinical examination, a palpable lump of size 8x7 cm with bilateral axillary lymphadenopathy was present. CECT abdomen showed multiple target lesions in the liver suggestive of metastasis & right adrenal metastasis.

Other investigations: Hemoglobin was 13.2gms%, total count and differential count were within normal limits, platelet count was 1.4 lakhs/cumm. Blood sugar, serum creatinine, blood urea and serum electrolytes were within normal limits. ECG & 2D Echocardiography were normal.

After NAT, on clinical examination, nipple retraction was present with no other visual abnormalities. On palpation, there was no palpable mass in breast, no axillary lymphadenopathy, no bony tenderness or organomegaly.

Ultrasonography of breast showed 4x3 cms ill-defined infiltrating mass. USG abdomen showed liver size of 15.3cm with mild fatty change, and well-defined hypo-echoic lesions of 1.8 cm size present in both right and left lobes. Gall bladder: nil particular. Left kidney showed calculi present in lower pole.

Grossly, received modified radical mastectomy specimen measuring 12x10x4 cm, with 9x6x4 cm axillary pad of fat and elliptical skin measuring 8x5cm along with intact nipple. On cut section, firm to hard, focal grey white areas with irregular streaks into the surrounding fat were present close to the posterior margin. (Fig. 1) No clear cut tumor was identified. Five lymph nodes were identified in axillary pad of fat, largest one measuring of size 1x1cm. Cut section of 3 lymph nodes showed grey-white in color and the remaining two were grey-tan in color.

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On microscopic examination, multiple sections showed normal breast tissue with tumor composed of small clusters, cords and sheets of tumor cells separated by fibro collagenous stroma. The individual tumor cells were pleomorphic, round to oval cells with eosinophilic cytoplasm with vesicular nucleus and prominent nucleoli. (Fig. 2, 4)

Stroma was infiltrated by chronic inflammatory cells consisting of mostly lymphocytes. Tumor giant cells and foci of necrosis was seen. At some focal areas tumor cells with cytoplasmic vacuolization & nuclear smudging was present (Fig. 3, 5). Foci of cholesterol clefts were also seen (Fig. 6).

Five lymph nodes showed metastatic deposits (post chemotherapy partial response) (Fig. 7). A diagnosis of Infiltrating duct cell carcinoma with post chemotherapeutic changes & metastatic deposits in lymph nodes was given.

DISCUSSION: Breast carcinoma is the most common non-skin malignant lesion in women after 4th to 5th decade of life. Clinically, patients present with a lump in the breast and the most common site is upper outer quadrant area of breast. Microscopically, it is classified into in-situ and invasive carcinomas and among invasive carcinomas, most common is invasive duct cell carcinoma "no special type".⁽²⁾

The treatment is simple mastectomy or modified radical mastectomy with axillary lymphnode dissection followed by chemotherapy or radiotherapy depending upon staging, ER, PR and HER2/neu status.

For the last 25 years there has been a revolution in the understanding of biological nature of carcinoma of breast. It is now accepted that the outcome of treatment is predetermined by the extent of its micrometastasis at the time of diagnosis. Variations in the radical extent of the local therapy might influence local relapse, but probably do not alter the long term mortality from the disease.⁽³⁾

As a result many international trials& analyses stated that appropriate use of adjuvant chemotherapy or hormonal therapy will improve relapse free survival.⁽³⁾ The aim of this NAT is to reduce tumor burden before surgery.^(4,5) NAT will shrink the tumor size. so that the pathologist cannot find any remaining malignant tissue during surgery which is called pathologic completed response (pCR) which correlates with prolonged survival.⁽⁶⁾

The several advantages of NAT are assessment of the efficacy of systemic therapy, tumor response a short term end point for clinical trials and increased eligibility for breast conservation and research linking tumor response to tissue sampling is facilitated.

It is very important to note the following observations.

1. Pathological changes in breast cancers after treatment.
2. Systemic response to treatment.
3. Recommendations for pathological examination and reporting.

NAT reduces the size of the primary tumor such that it is very difficult to identify the tumor on palpation. Microscopically, there is a decreased cellularity, tumor cells arranged in islands within tumor bed.⁽¹⁾

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Some tumors may appear to be higher grade or rarely lower grade due to cytomorphological changes from NAT. A change in tumor grade can only be assessed by comparing the post treatment tumor to the pre-treatment biopsy to treatment effect.^(1,6,7) The lymph node status is also an important prognostic factor in patients who receive NAT. The response in breast & lymph nodes is generally similar but evaluation of treatment response in lymph nodes is more complicated.⁽⁸⁾

Not all of a patient's lymph node metastases will respond equally to chemotherapy. Some nodal metastases with good response may not have any evidence of prior tumor involvement or may show fibrous scarring with little or no residual carcinoma, whereas other nodes may show large metastases after treatment.

In the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-18 at 9 years of follow up, patients with negative nodes or micro metastases, who were not treated with chemotherapy before surgery had identical survival, whereas those patients with macro metastases had a significantly worse survival. However, after NAT survival of patients' minimetastases and micro metastases in lymph nodes was similar to that of macro metastases and worse than that of negative nodes.

NSABP B-18 category, Miller-payne system. Chevallier method, Satal off method, RCB System and AJCC "y" Classification are used to determine the post chemotherapeutic changes after chemo therapy.

Pathological examination of the excised tumor bed is gold standard to identify a pathological complete response (pCR) to treatment or partial response to treatment.

The pretreatment specimen will be a core needle biopsy, because 15% to 28% of patients will have no residual tumor after NAT. It is important to have an adequate pretreatment sample in which invasive carcinoma is established and evaluation of hormonal receptors and HER2/neu status is completed before treatment. It is helpful to include histological type, grade, minimal size, presence of tumor necrosis and lymphovascular invasion to enable comparison of these features to the post treatment carcinoma.⁽⁹⁾

The following clinical information needs to be provided to the pathologist.

1. Presentation of the lesion before treatment.
2. Size of the lesion.
3. Prior diagnostic procedure: core biopsy or incisional biopsy specimen should be available for the comparison with the post treatment carcinoma.
4. Presence of clip or calcifications in the tumor.
5. Prior evaluation of lymph node and the results.
6. Type of NAT.
7. Clinical /radiological response of the carcinoma to the treatment (complete, partial, minimal).

Identification of primary tumor is important to determine whether or not the patient has had pCR and to allow localization for breast preservation. In case of pCR it is very difficult to identify the lesion grossly but microscopically may reveal substantial residual tumor. When calcifications are associated with tumor, they usually remain even after treatment and can be detected on specimen radiographs.

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Microscopic examination of tumor bed is characterized by areas of hyalinized vascular stroma with stromal oedema and fibroelastosis without the presence of normal breast tissue. The stroma is infiltrated by sheets of foamy histiocytes, aggregates of lymphocytes and hemosiderin pigment. Areas of tumor necrosis and cholesterol clefts are also present.

Some tumors show changes of treatment effects which include distortion of glandular architecture, enlarged tumor cells with enlarged cytoplasm, cytoplasmic vacuolization, eosinophilic change, pleomorphic and bizarre nuclei and decreased mitotic activity. Tumor cells are arranged in small clusters or singly and the cells shrink away from the stroma and might be misinterpreted as lymphovascular invasion.

It is preferable to sample the entire tumor bed with a rim of normal tissue to ensure there is no residual tumor. The axillary tail should be carefully searched for lymph nodes and all lymph nodes should be sampled. In general after NAT, lymph nodes become atrophic and fibrotic and difficult to be identified. In such cases, the fibrotic areas in the fat and tissue around the blood vessels should be sampled.⁽¹⁾

Lymph node metastases that show complete response to treatment often replaced by hyaline stromal scars, mucin pools or aggregates of histiocytes without any tumor cells. Whereas in cases of partial response the lymph nodes show islands or clusters of tumor cells within the hyalinized stroma.

CONCLUSION: Pathologists play a key role, in the evaluation of pathologic response, which is extremely important as a prognostic factor, for individual patients as a short term end point for clinical trials and as an adjuvant for research studies. So, surgical pathologists must be familiar with gross examination, sampling and reporting of breast carcinoma after NAT.

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Fig. 1: Gross photograph of mastectomy specimen measuring 12x10x4 cm. Cut section - ill defined, irregular, firm, greyish-white areas.



FIGURE 1

Fig. 2: Microphotograph showing sheets of pleomorphic tumor cells separated by stroma. (post chemotherapy partial response) H & E 100x.

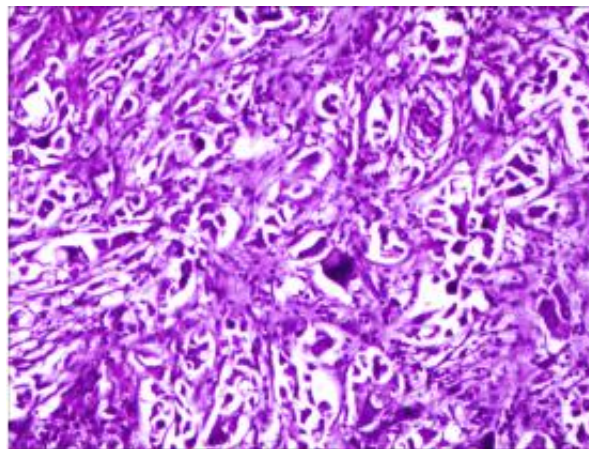


FIGURE 2

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Fig. 3: Microphotograph showing sheets of pleomorphic tumor cells with cytoplasmic vacuolization and pleomorphic bizarre nuclei. H & E 100x.

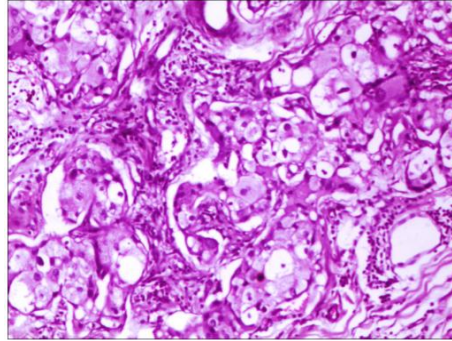


FIGURE 3

Fig. 4: Microphotograph showing sheets of pleomorphic tumor cells with hyperchromatic nuclei. H & E 400x.

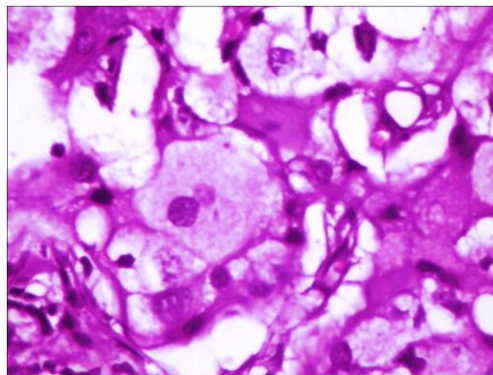


FIGURE 4

Fig. 5: Microphotograph showing sheets of pleomorphic tumor cells with foci of nuclear smudging. H & E 400x.

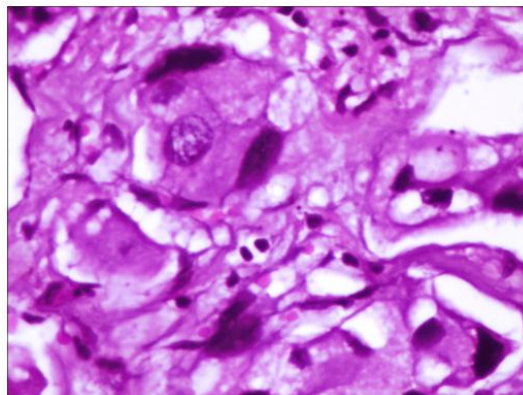


FIGURE 5

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Fig. 6: Microphotograph showing foci of cholesterol clefts. H & E 100x.

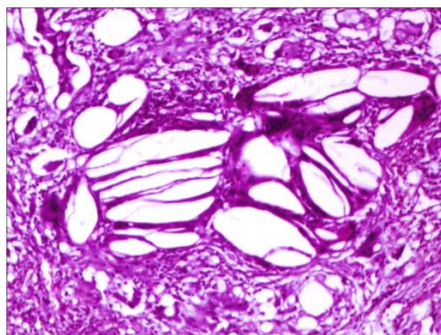


FIGURE 6

Fig. 7: Microphotograph showing lymph node with (post chemotherapy partial response) metastatic deposits. H & E 100x.

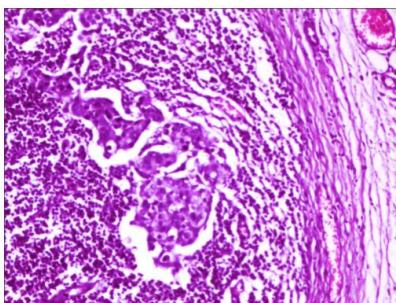


FIGURE 7

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