ORIGINAL RESEARCH PAPER

Pathology

A PILOT STUDY OF STATUS OF QUADRUPLE MARKERS IN CARCINOMA BREAST- A RETROSPECTIVE STUDY IN A TERTIARY CENTER

KEY WORDS:

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ABSTRACT

Introduction: Breast cancer is the most common malignancy of women. Most commonly it presents as painless lump in a middle aged women. The present study has undergone to study the incidence of triple negative status of carcinoma breast as it carries poor prognosis. **Material and methods:** In the present study, total number of cases included is 30. All the cases have undergone ER,PR, Her-2-Neu, Ki-67, Androgen receptor by immunohistochemistry method. The cases where Her-2-Neu is equivocal, FISH test has been done for confirmation. Androgen receptor staining done by IHC. Out of 30 cases, 28 cases shows AR negative and only two cases show AR positive. **Results and discussion:** Total cases included are 30. Out of 30 cases, 08 cases show triple negativity (ER-Negative, PR-Negative, Her-2-Neu- negative). So, 25% of cases show triple negativity. Conclusion: Significant cases of 25% are triple negative, hence carry poor prognosis and requires aggressive therapy.

Introduction:
Breast cancer is the most common malignancy of women. Most commonly it presents as painless lump in a middle aged women. Usually the most common location is the outer upper quadrant. However any part of the breast can be involved by the malignancy. All the breast lumps are diagnosed by multimodality approach which includes Ultrasonogram, Mammogram, Fine needle aspiration cytology and Tru Cut biopsy. However, Tru cut biopsy is the gold standard and confirmation test for the diagnosis of carcinoma breast1. It is followed by the standard protocol of treatment i.e Modified radical mastectomy with axillary clearance. Further management depends on the status of Hormone receptor present on the surface of tumor cells i.e Estrogen receptor, Progesterone receptor, Her-2-neu receptor. The present study has undergone to study the incidence of triple negative status of carcinoma breast as it carries poor prognosis2.

Materials and methods:
In the present study, total number of cases included is 30. All the cases have undergone ER,PR, Her-2-Neu, Ki-67 by immunohistochemistry method. The cases where Her-2-Neu is equivocal, FISH test has been done for confirmation.

Duration of study was 6 months

Inclusion criteria:
All the cases were reviewed by two pathologists.

Exclusion cases:
DCIS cases have been excluded

Results:
All the 30 cases have been properly evaluated. All the slides have been reviewed by two pathologists.

The follow are the observed results of the present study.
1. Mean age of the patient: 54 yrs (27 yrs to 80 yrs)

2. Status of Menopause: 60% of the cases have attained menopause.

3. Mean tumor size is 4.2 cm (Range: 1.5cm – 7.5cm)

4. Staging of tumors: T1- 05%, T2 – 67% , T3- 28%

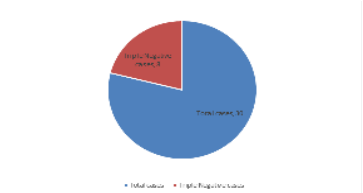
5. Modified Bloom's Richardson grading: Grade I- 30%, Grade II- 57%, Grade III- 13%

6. Immunohistochemistry: Total cases included are 30. Out of 30 cases, 08 cases show triple negativity (ER-Negative, PR-Negative, Her-2-Neu- negative). So, 25% of cases show triple negativity.

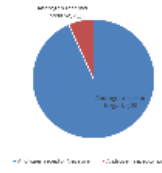
7. FISH test is done in 6 cases which show Her-2-Neu negativity as equivocal. FISH test is done for confirmation.

8. Androgen receptor staining done by IHC. Out of 30 cases, 28 cases shows AR negative and only two cases show AR positive.

8. Treatment history: All the patients have undergone Modified radical mastectomy with axillary clearance. 09 patients require adjuvant chemotherapy. The Adjuvant therapy used is CAF- Cytosine + Adriamycin +5-Fluorouracil.



Graph 01- It shows distribution of triple negative cases among total cases.



Graph 02- It shows distribution of androgen receptor status

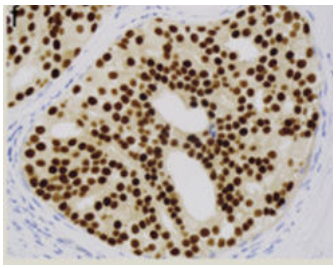


Image 01: IHC image for estrogen receptor.

Discussion:
Immunohistochemistry of breast carcinoma is a routine investigation done now-a-days for all the breast malignancy. The approach for the treatment of such patients depends on the expression of various receptor in tumor cells. The expression of estrogen receptor, progesterone receptor and Her-2-Neu is routinely done for all the breast carcinomas.

In 2010, for the first time, the American College of Pathologist has put forth the guidelines for the interpretation of estrogen and progesterone receptor. The guidelines aim at improving the diagnostic accuracy and clinical usefulness for the treatment of breast carcinomas.

Estrogen receptor(ER) is expressed on nuclear surface. Its interpretation contains two component, proportion of cells positivity and intensity of staining. Among the proportion, expression of estrogen receptor < 1% of cells are considered as negative. For ER positivity, 1-100% of tumor nuclei should be positive. Expression of Estrogen receptor in 1-10% of tumor nuclei are considered as Low positive.

Similar concept will apply to progesterone receptor. It is a nuclear receptor. Its expression in between 1-100% will be considered as positive. Expression of tumor cells <1% is considered as Negative. [3,4]

Human epidermal growth factor receptor 2 (HER2) is a protooncogene. It has tyrosine kinase activity. The gene is located on chromosome 17. Her-2-Nue overexpression is associated higher grade of breast carcinoma, Hence it acts as a poor prognostic factor. The patient with Her-2-Neu overexpression responds to anthracycline-based chemotherapies. It is also indication for starting the monocloncal antibodies like trastuzumab, pertuzumab etc. [5,6]
Her-2-Neu is interpreted as per 2018 ASCO/CAP guidelines. It is interpreted as mentioned below-

Score 0 : Negative: No staining observed/ Incomplete membrane staining that is faint or barely perceptible and within ≤10% of the invasive tumor cells.

Score 1+: Negative: Incomplete membrane staining that is faint or barely perceptible and within >10% of the invasive tumor cells.

Score 2+: Equivocal: Weak to moderate complete membrane staining observed in >10% of tumor cells.

Score 3+: Positive: Circumferential membrane staining that is complete, intense, and in >10% of tumor cells[7]

Androgen is steroid receptor located in nucleus. It is precursor for estrogen receptor. Almost 50% of breast cancer patient express the androgen receptor. It act as a source of estrogen in postmenopausal state. It is expressed as % of tumor cells positive for androgen receptor antibody. [8,9]

Triple negative status means the tumor cells of breast carcinoma are negative for Estrogen receptor, Progesterone receptor and Her-2-Neu receptor. In such tumors, there is no role of targeted therapy. Such patients have to undergo neoadjuvant therapy. Relapse rates are more in triple negative cases. [10,11]

In our study, 25% of cases show triple negative status in carcinoma breast. This incidence is correlating with other study. The meta-analytical study conducted by Akthar M and Sarkar S, it has large cases of 9787 in 10 years. Out of these cases, 25% cases are triple negative. [12] According to Kulkarni et al, it also shows the similar incidence of 275 of triple negative breast cancer. [13]

In our study, 8-10% of cases show androgen receptor positivity. But the literature shows higher incidence among the Indian population compared to our study. According to Anand et al study, the incidence of androgen receptor positivity is 56% among the Indian population. [14]. According to Mishra et al study, the incidence of androgen receptor positivity is 45-50% among the Indian population. [15].

Conclusion:
In the present study, the incidence of triple negative status in breast carcinoma is 25%, which is similar to overall Indian population, whereas androgen receptor status in this area is low when compared to overall Indian population.

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