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Original Research Paper

General Surgery

A STUDY OF MODALITIES OF MANAGEMENT DEPENDING ON IHC ER PR STATUS IN CARCINOMA OF BREAST

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ABSTRACT Breast Cancer is considered to be a multifaceted disease with diverse natural history, presenting with a varied spectrum of clinical, pathological, and molecular features with different prognostic and therapeutic implications. Recent attention has been directed singularly at molecular classifications of breast cancer. Despite the prognostic information provided by the molecular test, current reports of assay results impart little specific guidance of response to targeted and proven therapy. Apart from lending itself to subtype analyses of tumor when fresh tissue is not available, the IHC classification has prognostic and therapeutic implications, is inexpensive and readily available. In this prospective observational study breast cancer patients are classified based on the IHC profile ER/PR and Her2 neu expression, positive (+) or negative (-) and the modalities of management undertaken by those groups of patients. The incidence of IHC ER, PR and Her2 neu receptor positivity in the carcinoma of breast patients and its association with the prognosis and the modalities of management undertaken by these group of patients. Based on the patient profile in this study, it is concluded that the age group of the patients range from 30-80 Years, and that the left breast was more commonly involved by the malignancy. Based on IHC profile of breast cancer, it is concluded that Percentage of hormone receptor positivity for ER/PR in this study was 48%; Percentage of Her2 neu positivity in this study was 32%. In the present study ER/PR+, Her2- subtype was the most common. Based on the modalities of treatment, it is concluded that Majority of the patients included in the study were given chemotherapy and radiotherapy following surgery. ER/PR+, HER2+ and ER/PR+, HER2- subgroups of the patients responded better to the treatment with good prognosis.

KEYWORDS : Breast Cancer, Hormonal Receptors, Breast Cancer Treatment

INTRODUCTION

Over the last few decades there have been outstanding advances in molecular biology and in breast cancer management leading to earlier detection of disease and the development of more effective treatments resulting in significant declines in breast cancer deaths and improved outcomes for women living with the disease. Breast cancer is no longer seen as a single disease but rather as a multifaceted disease comprised of distinct biological subtypes with diverse natural history, presenting a varied spectrum of clinical, pathologic and molecular features with different prognostic and therapeutic implications. Consensus regarding the definitive prognostic/predictive analysis has yet to be reached, but significant progress continues to be made in the ongoing search for a specific, rigorous and reproducible method of identifying successful treatment algorithms utilizing biological markers.

Recent attention has been directed singularly at molecular classifications of breast cancer. While molecular and genetic testing is very elegant, prognostic and predictive, it is expensive and not yet widely available. Also, despite the prognostic information provided by the molecular test, current reports of assay results impart little specific guidance of response to targeted and proven therapy; for example, endocrine and trastuzumab therapy for tumours expressing oestrogen receptor/progesterone receptor (ER/PR) or human epidermal growth factor receptor 2 (Her2) proteins, respectively. The immunohistochemistry (IHC) classification provides both therapeutic and prognostic information.

In this study breast cancer patients are classified based on the IHC profile ER/PR and Her2 neu expression, positive (+) or negative (-) and the modalities of management undertaken by those groups of patients.

In the present study, breast cancer has been classified using IHC into 4 global subtypes out of the 8 possible subtypes commonly used by other authors. This classification is practical, simple, informative, clinically useful, and quite discriminative between the subtypes. The other four groups will emerge if differentiation is based on PR expression (ER+/PR+ vs. ER+/PR– tumours).

In this study, tumours have been divided into 4 groups according to IHC. IHC groups are:

1. ER/PR+, HER2+ : ER+/PR+/HER2+
   ER+/PR-/HER2+
   ER-/PR+/HER2+
2. ER/PR+. HER2- : ER+/PR+/HER2-
   ER+/PR-/HER2-
   ER-/PR+/HER2-
3. ER/PR-, HER2+ : ER-/PR-/HER2+
4. ER/PR-, HER2- : ER-/PR-/HER2-

The IHC classification correlates well with intrinsic gene expression microarray categorization: ER/PR+,Her2+ with Luminal B; ER/PR+,Her2- with Luminal A; ER/PR-, Her2+ and ER/PR-,Her2- with triple negative/basal-like tumours.

Apart from lending itself to subtype analyses of tumor when fresh tissue is not available, the IHC classification has prognostic and therapeutic implications, is inexpensive and readily available.

Methodology

This is a prospective observational study. We have studied 50 cases of locally advanced breast cancer which have undergone breast cancer surgery at the Department of General Surgery, Osmania General Hospital from November 2018 to August 2020. The clinical, operative and pathological data for all breast cancer patients was collected.

Name of the patients, pathology report and medical record

were identified then checked for proper clinical information such as age at diagnosis, menopausal status, clinical stage, tumor size and axillary lymph node status, histological subtypes and tumor grade (Scarf-Bloom-Richardson).

Patients with and inflammatory cancer or incomplete medical record were excluded.

After review, invasive carcinoma was selected for staining for the biomarkers. Total 50 cases were selected according to our inclusion criteria during the period of study.

ER and PR status studied by immunohistochemical analysis and recorded as positive and negative.

HER2 neu status studied by immunohistochemical analysis and recorded as 0,1,2,3. 0 and 1 are considered as negative, 3 is considered as positive. Patients with 2 were undergone FISH to know HER2 neu status.

Study Design

The incidence of IHC ER,PR and Her2 neu receptor positivity in the carcinoma of breast patients and its association with the prognosis and the modalities of management undertaken by these group of patients. The groups are:

- ER/PR+,Her2+ = ER+/PR+,Her2+;ER-/PR+,Her2+; ER+/PR-,Her2+
- ER/PR+,Her2- = ER+/PR+,Her2-; ER-/PR+,Her2-; ER+/PR-,Her2-
- ER/PR-,Her2+ = ER-/PR-,Her2+
- ER/PR-,Her2- = ER-/PR-,Her2-

Data Collection

Data on patients demographics, tumor characteristics, cancer stage at diagnosis, specifics of treatment (surgery, hormonal therapy, radiation, and chemotherapy), recurrence date and location of recurrence, date of death. Tumor size was determined from clinical measurement, mammographic measurement or surgical pathology.

The baseline workup will include clinical examination, bilateral mammography, and breast ultrasound.

After physical examination and radiologic studies (mammography, ultrasonography, MRI), core or incisional biopsies will be performed for histopathologic diagnosis.

Chest radiography, abdominal ultrasonography, bone scintigraphy, computed positron emission tomography (PET-CT), thorax and abdominal computed tomography (CT) were among the modalities that were used in systemic staging to look for distant metastasis.

Inclusion Criteria

- Postmenopausal females with locally advanced breast cancer.
- STAGE IIIA-IIIB DISEASE.
- Only patients who had initial pathologic testing at our center will be included.
- Patients with insufficient tumor tissue in post-surgical material, either due to complete pathological response or an insufficient number of remaining tumor cells, and patients who lost regular follow-up and patients with primary inflammatory carcinoma were excluded.

Exclusion Criteria

- Premenopausal females
- Unavailable ER, PR and HER2 status for the primary tumor
- Male sex
- A concurrent malignancy (non breast cancer)
- One time consultation with no follow up data
- Metastatic disease at the time of diagnosis
- Inflammatory breast cancer

RESULTS

1. Mean age of the patients in our study was 55.86. There was no statistically significant correlation with the receptor subtypes.
2. In our study 46% of the patients had right sided breast cancer while 54% had left sided breast cancer. There was no statistically significant correlation (p value-0.2840) of the breast cancer by site of the breast cancer.
3. In our study 54% of the total 50 patients had N1 disease and 32% of the patients had N2 disease, 10% had node negative disease and 4% had N3 disease.
4. In our study 52% patients had Stage III disease while 42% patients had Stage II disease, 4% patients had Stage I disease and 1% had Stage IV disease.
5. In our study 36% patients had moderately differentiated disease while 26% had well differentiated disease and 38% had poorly differentiated disease.
6. In our study 48% of the patients were ER/PR+ while 52% of the patients were ER/PR –VE and 32% of the patients are HER2 receptor positive and 68% of the patients are HER2 receptor negative.
7. In our study out of 50 cases ER positivity was shown by 22(44%) patients, PR positivity by 21(46%) patients and HER2 neu positivity by 16(32%) patients.
8. In our study out of 50 cases, 6(12%) were triple positive and 16(32%) were triple negative.
9. In our study, there was no statistically significant correlation of the age group with the receptor subtype.
10. In the present study, there was no statistically significant correlation (p value- 0.2840) of the side of breast cancer by receptor subtypes.
11. In our study, 100% of the N3 patients are there in ER/PR- type with 50% each in ER/PR-, Her2+ and ER/PR-, Her2-. 56.25% of the ER/PR-, Her2- patients had N2 disease, while 55.55% of the ER/PR+, Her2- patients had N1 disease. 30% and 16.66% of the ER/PR-, Her2+ and ER/PR+, Her2+ had N2 disease. The above observations suggest patients with ER/PR-, Her2- receptor subgroups had aggressive nature of the nodal disease.
12. In our observations of the total 6 ER/PR+,Her2+ subtype of patients 50% had stage III disease, of the total 18 ER/PR+,Her2- subtype of patients 33.33% had stage III disease. Of the total 10 ER/PR-,Her2+ subtype of patients 70% had stage III disease; of the total 16 ER/PR-,Her2- subtype of patients 62.5% had stage III disease. Out of 50 patients in the study 1 case had Stage IV disease that belongs to ER/PR-, Her2- subtype. The above observations suggests that patients with ER/PR-, Her2- subgroups had advanced stage of the disease compared to other subgroups p value (0.0405).
13. In our study, patients with ER/PR-,Her2+ and ER/PR-,Her2- subtypes had poorly differentiated (grade III) disease in 60% and 56.25% respectively while majority of the patients with ER/PR+,Her2- subtype had grade I(50%) and grade II(38.89%) disease. Above findings are suggestive of high incidence of well differentiated histology of tumor in patients with ER/PR+, Her2- subtype.
14. In our study, 92% of the patients were given chemotherapy and 88% were given Radiotherapy. All the patients (100%) who were ER/PR+ were given Hormonal therapy and only 25% of the Her2+ patients were given Herceptin treatment.

Summary

- In this study total 50 cases of carcinoma of breast which have undergone breast cancer surgery at the Department of General Surgery were included.
- Limitations of the present study are multifocality of tumor and recent molecular markers (ki-67, p53, plasminogen activator) were not included.
- Mean age of the patients in our study was 55.86. There was no statistically significant correlation with the receptor subtypes.

- There was no statistically significant correlation of the receptor subtypes of the breast cancer by site of the breast cancer (p value-0.2840).
- 54% of the total 50 patients had N1 disease and 32% of the patients had N2 disease followed by 10% with N0 disease and 4% with N3 disease.
- Most of the patients with ER/PR-, Her2- receptor subgroups had aggressive nature of disease.
- 52% of the patients had stage III disease followed by 42% with stage II disease and 4% of the patients with stage I disease and 1% with stage IV disease.
- Patients with ER/PR-,Her2+ and ER/PR-,Her2- subtypes had poorly differentiated (grade III) disease in 60% and 56.25% respectively while majority of the patients with ER/PR+,Her2- subtype had grade I(50%) and grade II(38.88%) disease.
- 48% of the patients were ER/PR+ while 52% of the patients were ER/PR –VE and 32% of the patients are HER2 receptor positive and 68% of the patients were HER2 receptor negative.
- Of the total 50 patients 6(12%) were of ER/PR+, Her2+; 18(36%) were of ER/PR+, Her2-; 10(20%) were of ER/PR-,Her2+; 16(32%) were of ER/PR-,Her2- subtypes.
- Of the total 50 patients 46(92%) patients received chemotherapy, and 44(88%) received radiotherapy while 24(100%) received hormonal therapy. Treatment with Herceptin i.e. Trastuzumab is taken only by 4(25%) patients.

CONCLUSION

Based on the patient profile in this study, the following conclusions could be arrived at

- The age group of the patients range from 30-80 Years, with a mean age of 55.86 years
- The left breast was more commonly involved by the malignancy than the right breast.

Based on IHC profile of breast cancer in this study, following conclusions could be made

- Percentage of hormone receptor positivity for ER/PR in this study was 48%.
- Percentage of Her2 neu positivity in this study was 32%.
- Percentage of ER positivity in this study was 44%.
- Percentage of PR positivity in this study was 42%.
- Percentage of triple positive cases was 12%.
- Percentage of triple negative cases was 32%.
- In the present study ER/PR+, Her2- subtype was the most common.

Based on the modalities of treatment in this study, following conclusions could be arrived at

- Majority of the patients included in the study were given chemotherapy and radiotherapy following surgery.
- The patients with ER/PR receptor positive were given Hormonal therapy in addition.
- The patients with Her2 receptor positive were given Herceptin(Trastuzumab)
- ER/PR+, HER2+ and ER/PR+, HER2- subgroups of the patients responded better to the treatment with good prognosis.

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