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Estrogen, Progestrone Receptor and Her2/Neu Expressions incases of Breast Cancer

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ABSTRACT

To correlate ER, PR and HER2/neu expressions with established prognostic factors viz. type of tumour, tumour size, tumour grade, tumour necrosis, lymphovascular invasion (tumor emboli), and axillary lymph node metastasis status. To correlate immunehistochemical marker status (ER, PR and HER2/neu) with clinical details (age and sex) of patients. The investigative research of Progesterone receptor (PR), Estrogen receptor (ER), as well as HER-2/neu expressions in cases of developing breast carcinoma was carried out over a period of 2 years from June 2015 to May 2017 which included 101 breast cancer cases. Palpable breast lump with or without pain were most frequent complaints. Maximum number of breast cancer cases revealed involvement of left breast. It was found that ER and PR expression was strongly correlated. No significant association was found between the presence of ER, PR expression as well as the size of the tumor. ER and PR negativity was associated with breast carcinoma cases having axillary lymph node metastasis. Out of 101 breast cancer cases tumor necrosis was present in 38.61%. However, the occurrence or absence of tumour necrosis in ER, PR expression was not strongly linked. Tumor emboli were noted in 31.68% of cases. In case of breast cancer with tumor emboli decreased ER and PR expression was observed.

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INTRODUCTION

Breast cancer is the most common cancer among women in developing countries. Women in India have secondary breast cancer to cervical cancer [1]. In India, a significant number of patients suffer from high-grade tumors as well as negative tumors of hormone receptors [2]. Just about half the women with early breast cancer have been identified with local operative removal surgery and removed. The grouping of patients of whom the disease is intended of recur is also essential to be identified, and it is predicted that the individuals can benefit from systemic chemotherapy [3]. Hormone receptors, aside from being a predictive marker, play a role in identifying patients for selective therapy and may also be considered a positive prognostic marker.

Aim

To study the case of breast cancer, in a tertiary hospital the marking the status of Estrogen receptor (ER), Progesterone Receptor (PR) and HER2/neu hormone receptor expressions.

Objectives

To correlate ER, PR and HER2/neu expressions with established prognostic factors viz. type of tumour, tumour size, tumour grade, tumour necrosis, lymphovascular invasion (tumor emboli), and axillary lymph node metastasis status. To corre-

late immunehistochemical marker status (ER, PR and HER2/neu) with clinical details (age and sex) of patients.

Breast cancer is a heterogeneous disorder in both clinical and pathological aspects. As Sistrunk and MacCarty pointed out years earlier, "the lifespan of all patients having breast cancer can't be estimated as the extent of tumour ranges vary greatly and patients reactions vary as well." [4] Various prognostic and predictive factors have been defined in breast carcinoma. These include age, stage, tumor size, type of tumor, nuclear and histological grade, presence of necrosis, axillary lymph node metastasis, hormone receptor status such as ER, PR and HER-2/neu expression by Biganzoli et al. (2009) [5].

It has been accepted that the prognostic value of grading provided by the Nottingham method, which have reported consistent and repeated validation of histologic grading as a clinically useful tool [6]. In a study performed by Doussal et al. (1989) [7] on the predictive value of a Scarff Bloom- Richardson grade on 1262 patients with operating breast cancer, the 3 distinct parameters of the SBR were analysed and it has been observed that perhaps the difference in the duct development was the smallest indicator as well as the most significant mitotic index of surviving steps. The most commonly used grading scale was the Scarff-Bloom-Richardson (SBR), which measured the creation of duct glands as well as nuclear features of pleomorphism and mitotic indices [7]. Approximately one-half of all symptomatic invasive breast carcinomas (invasive ductal carcinomas) are poorly differentiated, and well-differentiated tumors are least common in this group. Among screen-detected invasive breast carcinomas, moderately differentiated tumors are most common (comprising approximately 40%), with well-differentiated and poorly differentiated carcinomas each constituting 30%, respectively [4].

The first assays of ER in breast cancer were introduced in the mid- 1970s and were performed on crude tumor cytosol derived by centrifugation after homogenization. Tumor cytosol were incubated with high specific- activity radiolabeled steroid (estrogen or progestin), and the results reported as femtomoles (fmol) of receptor protein per milligram (mg) of total cytosol protein. The most widely used definition of positivity was at least 10 fmol/mg protein, but some described levels of more than 3 to 9 as borderline positive and negative as less than 3. Several disadvantages of the DCC assay existed, including variable tumor cellularity and heterogeneity as well as the requirement for fresh or snap-frozen tissue. These assays provide an overall score for the entire fragment of the tumor including neoplastic and non-neoplastic cells and may give false results, depending on the relative proportion of cancer versus other cell types within the tumor by Harris et al. (2014) [8].

In a study done by King and Greene (1984) [9] using immunochemical assay showed that monoclonal antibodies localize the estrogen receptors in the nuclei of target cells. Their observations indicated that estrogen receptors reside primarily in target cells nuclei of estrogen sensitive tissues and tumors, both in the presence and absence of steroid, analogous what has been reported for Vitamin D and thyroid hormone receptors. Incidence of ER and PR positive tumors increases at 11.0% per year during pre-menopausal years and at 4.6% per year after natural menopause. By comparison, the prevalence in pre-menopautic condition and normal menopause of ER, as well as PR negative tumors, rises to 5.0% per annually [10].

In a study done on 784 females with primary breast cancer correlated ER and PR receptors found a significant relationship between age and the menopausal status. Mean age of ER positive tumor was 58.9± 0.6 years which was higher than ER negative and borderline with mean age 53.7± 0.7 and 51.6± 1.1 respectively. PR positivity also increases with age. They concluded that estrogen and progestrone receptor protein levels tend to increase as the women become menopausal. [11] A study done by McCarty et al. (1980) [12] on 500 primary breast cancer patients concluded that size of primary and extent of the disease did not have any significant association with the hormone receptor status.

In a study done by Pinder et al. (1998) [13] on 465 breast cancer patients found significant associations between lymph node negative disease and ER and PR status. They found that for both lymph node, higher grade lesions negative and positive tumors, etc. were more often larger and ER negative but was in a lower prediction category. High grading was related to PR negatives in the lymph node negative tumours.

MATERIALS AND METHODS

The research is a two year cross-sectional study examining the estrogen receptor (ER), progesterone receptor (PR) as well as the HER-2 / neu status of cases and their association with predictor variables. The study was carried out in the department of Pathology and Molecular and Genetics laboratory during a period of June 2015 to May 2017, which includes 101 cases.

Table 1: Correlations of ER with PR in breast cancer cases

Correlations of ER with PR in breast cancer cases		
	ER	PR
Positive	57	57
Negative	44	44
Total	101	101

Table 2: Axillary lymph node metastasis distribution in breast carcinoma cases

Axillary lymph node	Number of cases (%)
0	59 (58.41%)
1-3	22 (21.78%)
>3	20 (19.80%)
TOTAL	101 (100%)

Inclusion Criteria

All the breast cancer cases who underwent lumpectomy or mastectomy with informed consent.

Exclusion Criteria

Cases where only a trucut biopsy had been done were excluded. Cases with extensive tumour necrosis without sufficient viable tumour cells were excluded because they were not helpful for an accurate evaluation of the immunohistochemical result. Specimens of breast cancer (lumpectomy or mastectomy) were collected after surgery in 10% neutral buffered formalin and were fixed for 12 hours. Care was taken to prevent over fixation of tissue, as it would interfere with receptor interpretation.

Following fixation, the tissue was examined at tissue of three dimensions including the specimen's weight, the proportions of the surface, the presence or absence of a biopsy scar, the existence and position of the tumour, Prud' orange colour, and/or ulcerations of the nipples and/or skin around. Serial cut sections were taken. Tumor number, size, consistency, margins (pushing/infiltrating), evidence of tumor necrosis were noted. The distance of the tumor from the overlying skin, deep and peripheral surgical margins were noted. The deep surgical margin was painted with India Ink. An adequate number of sections were taken from tumor proper, tumor with deep surgical margin, nearest peripheral surgical margin, other peripheral surgical margins, adjacent breast tissue, overlying skin, nipple, areola and other significant areas. An extensive search for any intramammary lymph node or satellite tumor was done. Careful grossing of an axillary tail was done. Size of the largest lymph node was noted and all the lymph nodes were given for processing.

OBSERVATIONS AND RESULTS

The study of Estrogen receptor (ER) Table 1, Progesterone receptor (PR) and HER-2/neu expressions in cases of breast cancer was done in our institute with attached tertiary care centre. Total 101 breast carcinoma cases were obtained within a period of 2 years from June 2015 to May 2017, which was a hospital based cross sectional study.

When ER and PR status were analyzed, both were positive in 57 cases (56.43%) and negative in 44 cases (43.56%). A positive correlation existed between ER and PR expression.

Out of 101 cases of breast cancer cases, 42 cases (41.58%) revealed metastasis to an axillary lymph node. 21.78% cases showed 1-3 axillary lymph node involvement while 19.80% showed >3 axillary lymph node metastasis in Table 2.

DISCUSSION

Breast cancer is a clinically and pathologically heterogeneous disease. Various prognostic and predictive factors have been defined in breast carcinoma. IHC allows for the determination of receptor status at the individual cell level, accommodating the problem of tissue heterogeneity within the tumor. IHC technique is relatively simple, inexpensive, and familiar to most laboratories, and results in a permanent glass slide. The ER, PR and HER-2/neu expressions study for cases of breast carcinoma was carried out in our institute with attached tertiary care centre. Total 101 cases of breast cancer were obtained within a period of 2 years from June 2015 to May 2017, which was hospital based, cross sectional study. ER, PR and HER-2/neu receptors were correlated individually with each of the prognostic factors like age, tumor size, histological type and grade, axillary lymph node metastasis, lymphovascular invasion (emboli tumor) and tumor necrosis.

CONCLUSIONS

Estrogen and Progesterone receptor expression correlate well with the established diagnostic markers like- age of the patient, histological grade, type of tumor, axillary lymph node metastasis as well as emboli tumor. The reality that the majority of these cases will explain the low hormone receptors positive responses presented with large tumor size, having axillary lymph node metastasis and high grade histological features during diagnosis. It was found

that Estrogen and Progesterone receptors positivity and HER-2/neu receptor negativity is significantly correlated with lower grade of tumor. Triple negative breast cancer is seen in maximum cases of medullary carcinoma. ER and PR negativity is seen in the majority of breast carcinoma cases having axillary lymph node metastasis. Low ER and PR expression is seen in breast cancer cases with tumor emboli. Younger age group patients present with aggressive histopathological features and triple negative receptor status.

Conflict of interest

The authors declare that they have no conflict of interest.

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REFERENCES

[1] V M Bhagat, B M Jha, and P R Patel. Correlation of hormonal receptor and Her-2/neu expression in breast cancer: a study at tertiary care hospital in south Gujarat. *Natl J Med Res*, 2(3):295–303, 2012.

[2] Stanley P. L. Leong, Zhen-Zhou Shen, Tse-Jia Liu, Gaurav Agarwal, Tomoo Tajima, Nam-Sun Paik, Kerstin Sandelin, Anna Derossis, Hiram Cody, and William D. Foulkes. Is Breast Cancer the Same Disease in Asian and Western Countries? *World Journal of Surgery*, 34(10):2308–2324, 2010.

[3] P Shrigondekar, S Desai, S Bhosale, D Mankar, and A Badwe. Study of Hormone Receptor Status of Breast Carcinoma and Its Correlation with the Established Prognostic Markers. *Research Gate*, 1(2):109–116, 2020.

[4] S A Hoda. Invasive ductal carcinoma: assessment of prognosis with morphologic and biologic markers, Rosen's breast pathology, 4th edn. Philadelphia, USA, 413, 2014. Lippincott Williams & Wilkins.

[5] L Biganzoli, M Castiglione, and M J Piccart. Adjuvant Therapy for Breast Cancer. volume 151, pages 13–30. Springer-Verlag US, 2009.

[6] David L. Page, Ian O. Ellis, and Christopher W. Elston. Histologic Grading of Breast Cancer:Let's Do It. *American Journal of Clinical Pathology*, 103(2):123–124, 1995.

[7] V. Le Doussal, M. Tubiana-Hulin, S. Friedman, K. Hacene, F. Spyratos, and M. Brunet. Prognostic value of histologic grade nuclear components of Scarff-Bloom-Richardson (SBR). An improved score modification based on a multivariate analysis of 1262 invasive ductal breast carcinomas. *Cancer*, 64(9):1914–1921, 1989.

[8] Jay R. Harris, Marc E. Lippman, Monica Morrow, et al. Diseases of the breast: Fifth edition. pages 1–3. Wolters Kluwer Health Adis (ESP), 2014.

[9] W. J. King and G. L. Greene. Monoclonal antibodies localize oestrogen receptor in the nuclei of target cells. *Nature*, 307(5953):745–747, 1984.

[10] W C Willett, R Tamimi, S E Hankinson, A Hazra, A Eliassen, and G Colditz. Nongenetic factors in the causation of breast cancer. *Research Gate*, pages 221–253, 2014.

[11] Martin L. Lesser, Paul Peter Rosen, Ruby T. Senie, Kathleen Duthie, Celia Menendez-Botet, and Morton K. Schwartz. Estrogen and progesterone receptors in breast carcinoma: Correlations with epidemiology and pathology. *Cancer*, 48(2):299–309, 1981.

[12] Kenneth S. McCarty, Thomas K. Barton, Bernard F. Fetter, Brett H. Woodard, Jeffrey A. Mossler, William Reeves, John Daly, William E. Wilkinson, and Kenneth S. McCarty. Correlation of estrogen and progesterone receptors with histologic differentiation in mammary carcinoma. *Cancer*, 46(S12):2851–2858, 1980.

[13] S. E. Pinder, S. Murray, I. O. Ellis, et al. The importance of the histologic grade of invasive breast carcinoma and response to chemotherapy. *Cancer*, 83(8):1529–1539, 1998.