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HISTOPATOLOGICAL SPECTRUM OF BREAST CARCINOMAS AND CORRELATION OF HISTOLOGICAL GRADE WITH ER, PR, HER2NEU STATUS IN A TERTIARY CARE CENTRE OF EASTERN INDIA

Pathology

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ABSTRACT

Background: Carcinoma of the breast is a truly complex disease with a large intratumoral heterogeneity, leading to markedly variable clinical course and response to treatment modalities.
Prognosis and management of breast cancer are influenced by variables such as stage, grade, hormone receptor status of estrogen(ER), progesterone(PR) and Human epidermal growth factor receptor2 (HER2/neu) over expression.
Aims and Objectives: To highlight the histomorphological spectrum of breast carcinomas and their ER,PR, HER2NEU status. And also to find out correlation between their histological grade and the hormone status .
Materials and Methods - 115 breast carcinomas were clinicopathologically and immunohistochemically analyzed in which assessment of Her-2/neu, ER, PR had been performed prospectively. Statistical analysis was then used to correlate the above observation.
Conclusion: This study highlights the importance of histopathology and immunohistochemistry in breast cancers not only in diagnosing the lesion but also in predicting the prognosis and target therapy.

KEYWORDS

Breast Cancer variants, Grade, ER, PR and Her 2 neu, IHC.

INTRODUCTION

Invasive breast cancer is the most common carcinoma in women. It accounts for 22% of all female cancers, Invasive breast carcinoma is a group of malignant epithelial tumors of the breast characterized by invasion of adjacent tissues and a marked tendency to metastasize to distant sites, believed to be derived from the mammary parenchymal epithelium, particularly cells of the terminal duct lobular unit (TDLU).[1]

Breast carcinomas exhibit a wide range of morphological phenotypes and the histopathological types have particular prognostic or clinical characteristics.[2]

Hormone receptor studies such as estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor-2 (HER2/neu) are routinely done in breast carcinoma now. It not only helps in the prognosis of the tumor but also helps in deciding its treatment. The goal of doing this receptor status is to provide right treatment to the right patient.[3]

The objectives of our study are to evaluate ER, PR, HER2 NEU expression in different histological types of breast cancers with special emphasis on atypical breast carcinomas in our tertiary referral institution in Eastern India and whether there is any association between hormonal status and histological grade of the tumor.

Many studies have demonstrated a significant association between histological grade and survival in invasive breast carcinoma. It is now recognized as a powerful prognostic factor and should be included as a component of the minimum data set for histological reporting of breast cancer[4]

METHOD

This prospective study was done in the Pathology department of N.R.S. Medical College Hospital. Kolkata, West Bengal. Total 115 cases were studied in one year (January2018- April 2019). Among them 60 cases obtained from modified radical mastectomy, 25 cases from simple mastectomy, 10 cases from lumpectomy specimens and 15cases from tru cut biopsy. Metastatses from other sites have been excluded. All samples were subjected for routine histological examination , stained with Haematoxylin &Eosin stain and immunoistochemistry done with ER, PR, HER2NEU receptor markers.

ER,PR positivity was interpreted by Allred scoring system and HER2/neu positivity was interpreted and reported using ASCO 2007 guidelines (American Society of Cancer Oncology) which takes into account the cytoplasmic membrane staining and the proportion of immune positive tumour cells in comparison to positive controls.[3,4]

Assessment of histological grade was done by Modified Bloom and Richardson[5] grading system.

RESULTS

In this study, a total of 115 cases were studied with ages ranging from 21 to 79 yrs. Among them 43% cases appeared in the age group of 41-50 yrs. Figure 1

The commonest histological pattern noted was invasive breast carcinoma of no special type (90 cases), followed by 11 cases of invasive lobular carcinoma and 5 cases of medullary carcinomas and 5 cases of mucinous carcinomas and 1 each for metaplasic carcinoma, invasive papillary carcinoma, tubular carcinoma and paget's disease with invasive ductal carcinoma component. Figure 2

Among invasive breast carcinoma, no special type (IDC-NST), we got 2cases of IDC with apocrine changes and 2 IDC-NST with neuroendocrine features, and 1 solid papillary carcinoma with invasive component ,1 IDC-NST with osteoclast like giant cell rich type.

Figure 1

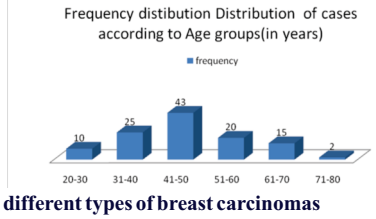

Figure 2 : different types of breast carcinomas

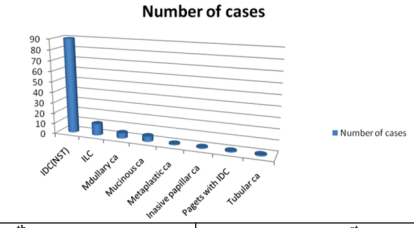

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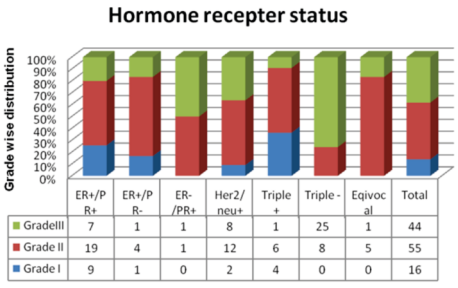
Figure 3

Hormone receptor status	Grade I NO. (%)	Grade II NO. (%)	Grade III NO. (%)	Total NO. (%)
ER+/PR+	9(25.7)	19(54.3)	7(20)	35(100)
ER+/PR-	1(16.6)	4(66.6)	1(16.6)	6(100)
ER-/PR+	0	1(50)	1(50)	2(100)
Her2/neu+	2(9)	12(54.5)	8(36.36)	22(100)
Triple +	4(36.4)	6(54.5)	1(9)	11(100)
Triple -	0	8(24)	25(75.)	33(100)
Equivocal	0	5(83.3)	1(16.7)	6(100)
Total	16(13.9)	55(49.3)	44(38.2)	115(100)

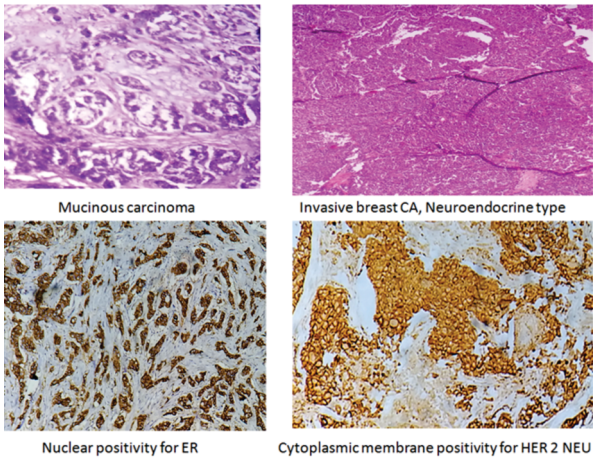
Figure 4



Out of total 115 cases, we got 16 grade I cases, 55 grade II cases and 44 grade III breast carcinomas. Among all, 35 breast carcinomas were ER/PR positive, 33 were triple negative, 22 cases were HER2/neu positive, 11cases were triple positive and 06 cases were HER2 equivocal (Figure 3).

In this study, out of the 16 grade 1 tumours, 56.5% cases were ER/PR positive and HER2/neu negative;. Also among grade III cases, 56.81% cases were triple negative tumors which have an aggressive behavior compared to other subtypes and were common in premenopausal women (Table 2).

Figure 5: Histopathological &Immunochemistry photographs of different breast carcinomas



DISCUSSION

Breast cancer is a heterogeneous disease with multiple subtypes, variable size, grade, metastatic potential and with varying prognosis. Hence, the choice of therapy for patients with breast cancer is to some extent defined by information provided by the pathological assessment.

On the basis of cell morphology, growth, and architectural patterns, breast cancer can be classified in up to 21 distinct histological types.[9] In this study, most of the breast carcinomas are of invasive breast carcinoma, no special type (78.2%) and most common age group affected is 5th -6th decade of life that corroborate with the study by Greeshma Ann George et al .[6]

In this study, majority of breast carcinoma were grade 2 (49.3%) followed by grade 3 (38.3%) and grade 1 (13.9 %) which were in concordance with the studies done by Azizun-Nisa et al and Ambroise et al; and Greeshma Ann George et al .[3,6]

It has been well established that endocrine manipulation is the cornerstone of therapy for hormone receptor-positive tumors; anti-HER2 agents combined with chemotherapy or endocrine therapy are the standard treatment for tumors overexpressing HER2. Chemotherapy represents the only approach for the treatment of triple-negative breast cancers,[7,13]

If a patient's tumor expresses ER and/or PR, we can predict that this patient will positively benefit from endocrine therapy such as tamoxifen. The overexpression of the oncogene HER2/neu in a patient's breast cancer is an example of both a prognostic and predictive biomarker. HER2/neu expression is associated with poor prognosis (high risk of recurrence; however, it also predicts that a patient will more likely benefit from anthracycline and taxane-based chemotherapies and therapies that target HER2/neu (trastuzumab), but not to endocrine-based therapies.[7,8,12]

In the present study good correlation was found between ER/PR hormone receptor status and grade of tumor. 80 % of all the ER/PR positive cases were of grade 1 and grade 2 breast cancers and 75 % of the triple negative cases were grade 3 breast cancers. This was in concordance with studies done by Azizun-Nisa et al and Geethamala K et al.[3,14]

Immunohistochemistry revealed 30.43 % ER/PR positive, 19.1% HER2/neu positive(ER/PR negative), 28.7% Triple negative and 9.5% Triple positive and HER2/neu equivocal tumors. These results were in concordance with the studies done by Adedayo et al and Sharif et al and were in discordance with a study done by Suvarchala et al, which had higher triple negative tumours (42.19%).[10,11]

In the present study good correlation was found between ER/PR hormone receptor status and grade of tumors.

The limitation of the present study was the absence of correlation with Fluorescent in situ Hybridization (FISH) studies in Her2/neu equivocal cases.

CONCLUSION

Breast carcinoma is the most common malignant tumor in women, and it is the leading cause of mortality worldwide annually.

Breast cancers are classified according to the histological features or molecular characteristics of the tumor. Each of them influences the outcome and response to the treatment.

Nowadays, in our daily clinical pathology practice, the clinical value of assigning invasive breast cancers beyond routine histologic type, histologic grade, and ER/PR/HER2 status has not been established.

In our study, most of the the grade 1 and grade 2 tumours were ER/PR positive and majority of grade 3 tumors were triple negative which exemplifies the fact that higher the histological grade, lower is the hormone receptor expression. Assessment of hormone receptors for clinical management of breast cancer patients is strongly advocated to provide prognostic information and best therapeutic options. Histological grading highly correlates with the survival rate and the receptor status predicts the response to hormonal therapy.

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