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Original Research Article

To correlate HER-2/neu status in invasive ductal carcinoma breast with histopathological grades of Nottingham score

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ABSTRACT

Background & Methods: The present study entitled "To correlate HER-2/neu status in invasive ductal carcinoma breast with histopathological grades of Nottingham score" was conducted in Dept. of Pathology, at SRMSIMS, Bareilly.
Result: Out of 56 cases all grade 1 tumour were negative for Her2/neu while in grade 2, 17 cases (43.58%) were positive for Her2/neu and in grade 3, 08 cases (80%) were positive for Her 2/neu.
Study Designed: Observational Study
Conclusion: Among all the 60 cases studied it was seen most of the cases with grade 1 tumor were positive for ER & PR receptors & carry better prognosis, while the grade 3 cases were mostly positive for Her2/neu & have poor prognosis. Positive Her2/neu expressed were mostly ER & PR negative & this shows inverse correlation among them.

1. Introduction

HER 2 (also referred to as HER 2/neu and erb 32) is a proto-oncogene located on chromosome 1713. It encodes a tyrosine-kinase receptor residing on a surface membrane of breast epithelial cells.[1] Many studies during the past 25 years have shown that the HER-2 gene is amplified in up to 30% IBC & that amplification is highly correlated with over expression of the protein.[2]

The relationship between HER-2/neu status and clinical outcome is complex & varies with the setting. There is weak but significant association between the poor outcome & positive HER-2/neu in patients receiving no additional therapy after initial surgery15. Most patients receive some type of adjuvant therapy & the association between HER-2 status & outcome seems to depend on type of therapy.[2] The most useful finding come from recent studies showing that HER-2 / positive tumors respond favorably to new antibody based therapies & the reason for assessing HER-2/neu Status today is to identify candidate for targeted therapy.[3]

There has been a long & persistent controversy about whether it is best to evaluate HER-2/neu status by measuring protein expression by IHC or gene amplification by FISH. Many studies have share that, when properly performed there is a very strong correlation between IHC & FISH & that they are equivalent in clinical utility.[4]

2. Materials and Methods

The present study entitled "To correlate HER-2/neu status in invasive ductal carcinoma breast with histopathological grades of Nottingham score" was conducted in Dept. of Pathology, at SRMSIMS, Bareilly.

This case study was prospective and retrospective. Prospective cases were selected from the patients admitted for surgery of invasive ductal carcinoma breast in Medical College Hospital. As regards retrospective cases, they were obtained from the histopathological records obtained from Pathology department of SRMS-IMS, Bareilly.

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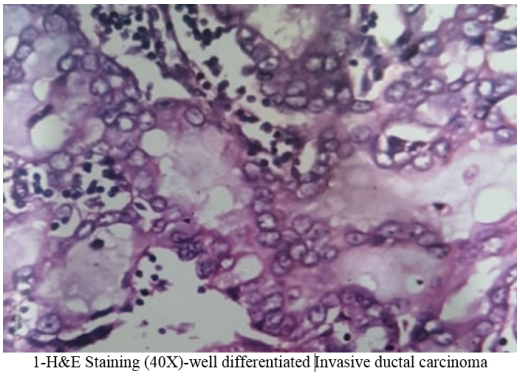
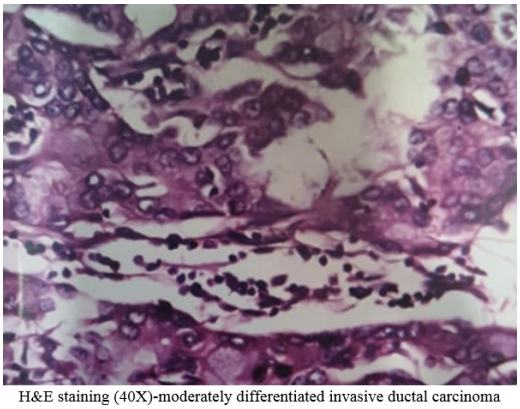
1. Biopsies and mastectomy specimens were fixed in 10% formalin.
2. Detailed history about age, family history, clinical diagnosis and chief complaints was enquired.
3. Tissue was fixed in buffered formalin for about 6 hour after adequate slicing.
4. Gross appearance of mastectomy specimen/biopsy was noted.
5. Paraffin blocks after thorough tissue processing were prepared.
6. Sections were cut 3-4 micron thick and subjected to following:
7. Routine haematoxylin and eosin staining was done for histological typing and grading of all cases.
8. Immunohistochemistry was done using labelled antibodies for hormone receptor status (Oestrogen receptor & Progesterone status), Her2/neu & proliferative index Ki-67.



1-H&E Staining (40X)-well differentiated invasive ductal carcinoma

Fig. 1: Well differentiated Invasive Ductal Carcinoma

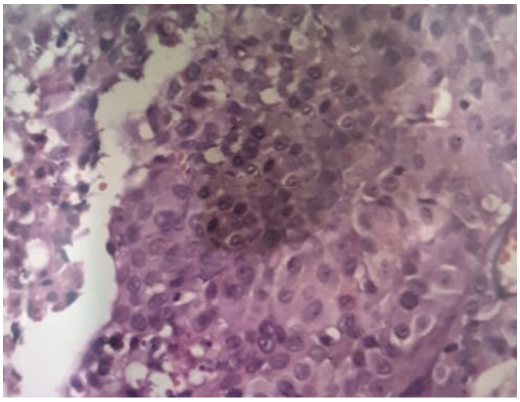


H&E staining (40X)-moderately differentiated invasive ductal carcinoma

Fig. 2: Moderately Differentiated Invasive Ductal Carcinoma

3. Results

Table 1 Her2/neu status was seen in all cases. Out of 56 cases, 31 cases (55.35%) were Her2/neu negative. 11 cases (19.64%) shows scoring 2 i.e. weakly positive & 14 cases (25%) were strongly positive.



H&E (40X)-Poorly differentiated invasive ductal carcinoma

Fig. 3: PoorlyDifferentiated Invasive Ductal Carcinoma

Table 1:

No. of cases (56)	HER2/NEU	Percentage
31	negative	55.35%
11	Weakly positive	19.64%
14	Strongly positive	28.57%

Table 2:

Grade of tumor	HER 2/NEU positive	Percentage	HER2/NEU Negative	Percentage
Grade 1(7)	0	-	7	100%
Grade 2(39)	17	43.58%	22	56.41%
Grade 3(10)	08	80%	02	20%

Table 2 Out of 56 cases all grade 1 tumour were negative for Her2/neu while in grade 2, 17 cases (43.58%) were positive for Her2/neu and in grade 3, 08 cases (80%) were positive for Her 2/neu.

Table 3:

Number of cases	ER & PR positive	HER2/neu	percentage
56	27	negative	48.21%
56	18	negative	32.14%

Here the value of ($p<0.0001$) which is significant.

On correlating Her2/neu status with hormone receptor status an inverse relation is seen. Out of 56 cases, 27 cases (48.21) which were ER & PR positive but Her2/neu was negative, 18 cases (32.14%) which were ER & PR negative showed positivity for Her2/neu.

4. Discussion

None of the hormone receptor assays are absolute in their ability to predict response. A proportion (0-10 % in different studies) of ER negative tumours are found to respond to hormone therapy.[5] It has been postulated that ER expression is stimulated by low levels of available estrogen[6] and it is possible that down regulation of the ER gene to immunohistochemically undetectable levels may occur in some tumour due to high circulating levels of endogenous estrogen. This does not necessarily mean that they will not respond to hormone therapy, which has itself been shown to up-regulate ER expression in normal breast tissue.

It was also seen in our study of all cases of invasive ductal carcinoma that expression of ER or PR was decreased significantly in HER2+ tumours in comparison to HER2- tumours. None of the grade 1 primary was HER2 + and majority of grade 3 tumours were HER2 +. The rate of ER & PR expression in nuclear grade 2 HER2+ tumours was significantly higher than in nuclear grade 3 tumours (ER & PR, $p < 0.0001$).[7]

It was also seen that that higher the grade of tumour more is proliferative index Ki-67. Most of grade 1 tumour shows Ki-67 20-30%, grade 2 tumours show Ki-67 30-60% and grade 3 tumours shows Ki-67 70-80%.

Many studies have shown high expression of Ki-67 as poor prognostic factor in breast cancer.[8]

Colozza & coworkers thoroughly reviewed 132 articles including 159,516 patients in regards to prognostic and predictive value of Ki-67 & other proliferation markers. The authors appropriately pointed out that all studies concerning these markers are level 4 or level 3 evidence at best.

However the number of cases in the present study is small and larger series of cases with long follows up is required to reach any definitive conclusion. Ultimate goal of each study is how it can be beneficial to the society. Any research by itself on breast carcinoma is useful because of the sheer numbers of women worldwide who suffer morbidity & mortality due to this disease. Hence there is relevance of search for new prognostic markers & also refining and redefining the currently in vogue IHC parameters to provide more useful prognostic information which may help in stratifying patients.

5. Conclusion

Among all the 60 cases studied it was seen most of the cases with grade 1 tumor were positive for ER & PR receptors & carry better prognosis, while the grade 3 cases were mostly positive for Her2/neu & have poor prognosis. Positive Her2/neu expressed were mostly ER & PR negative & this shows inverse correlation among them.

6. Source of Funding

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7. Conflict of Interest

The authors declare they have no conflict of interest.

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