

A Study Comparing Histopathological Grade of Breast Carcinoma with Her2/Neu Status in a Tertiary Care Hospital

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ABSTRACT

Introduction: Breast cancer is a leading cause of concern in today's medical care and newer diagnostic tools like immunohistochemistry have been frequently implemented in diagnostic efforts in addition to the existing histopathological findings. It is important to see how these two diagnostic modalities show up as a whole and in relation to each other. Through this study, we make an effort to accomplish just the same.

Aims and Objectives: To look at the observations and comparative findings of histopathological grade and immunohistochemical (HER2/neu) markers and find any correlation that may be of help to future studies.

Materials and Methods: A sample of 50 patients with Invasive breast Ca was observed and their histopathological grades (Nottingham scoring) were sent along with immunohistochemistry done (HER2/neu). Results and noted and tallied with each other.

Results: It was observed that there were maximum cases of grade 2 followed by 3 and then 1. Also that there were more HER2/neu negative cases than positive. Also that the frequency of HER2/neu positivity was more in grade 1 yet quantity of cases of HER2/neu positivity turned out to be more in grade 2.

Conclusion: It would be very helpful to keep a close eye on even lower grades of Breast carcinoma as they would have a high chance of HER2/neu positivity and thus poor prognosis.

Keywords: Breast; Carcinoma; HER2/neu; Histopathological; Grading; Immunohistochemistry

INTRODUCTION

India has around 2.25 million cases of breast cancer with over 1 lakh new cases being registered every year, according to Cancerindia.org. It has been estimated by ICMR that India will register over 17 lakh cases resulting to over 8 lakh deaths by 2020.

There are various types of breast cancer which differ in terms of their morphology and histological pattern. ⁽²⁾ Immunohistochemistry has opened up new horizons in the diagnosis of breast cancer. The classification calls for the detection of Estrogen receptors, Progesterone receptors and Human epidermal growth factor receptors HER2/neu. usually multiple parameters are studied together to get the most accurate prognostic and therapeutic information. ⁽¹⁾ Observations have been made in various studies which compare these IHC markers to variables viz. morphological types, grade, age, sex, etc.

AIMS AND OBJECTIVES

Objective of this study was to observe the frequency of various grades in Invasive Breast Carcinoma cases as well as that of HER2/neu positivity and to compare

the two findings in correlation with each other. As a result we can notice any common observational and comparative findings that may have been observed in the past and to verify them with relevant existing data.

MATERIALS AND METHODS

Our study contains the data for 50 patients collected over a period of 2 years. The said data was procured from the records of a reputed tertiary care hospital. We worked with multiple types of samples mainly -MRM's, core biopsies and lumpectomies.

These samples were then stained using IHC and H&E staining techniques. In H&E staining method we use hematoxylin for nuclear staining while acid alcohol helps in differentiation which is made evident by using eosin which is the counterstain. (3) In the case of IHC staining there is a complex procedure involved which calls for multiple washings of the sample with various buffers and use of chromogens and antibodies. (4-6)

Based on this data, we have compared the histopathological grade, based on Bloom Richardson scoring/ Nottingham scoring with the HER2/neu results and analysed.

RESULTS

The first table we have here with us gives us a general idea of the distribution of cases across the 3 grades. We can clearly see that the cases from grade 2 and 3 are significantly more than the lower grade 1. Also the maximum cases are of grade 2 which is closely followed by the number of cases in grade 3.

GRADE	NO. OF CASES	PERCENTAGE
I. (score 3-5)	4	8%
II. (score 6-7)	24	48%
III. (score 8-9)	22	44%
TOTAL	50	100%

The second table divides the cases on basis of their grade and HER2/neu findings. This data divides each histologic grade into two groups - HER2/neu positive

and negative. On a whole we can see that while maximum cases are of grade 2 as seen in the previous table, most of the cases are HER2/neu negative. On observing the HER2/neu positive cases we find that grade 1 though having the least number of cases; shows maximal percentage of positivity - 50%. Lowest values of HER2/neu positivity are seen in grade 3.

		HER2/neu findings		Total
		Positive	Negative	
Grade	1	2	2	4
	2	6	18	24
	3	2	20	22
Total		10	40	50

DISCUSSION (7-11)

According to our findings we found that even though the higher grades had more volume of HER2/neu positive cases the percentage of positivity was higher in grade 1.

Prati et al showed 58.7% of HER2/neu positive cases in grade 1, 58.1% in grade 2 and 54.5% in grade 3. This is similar to our findings where even though grade 2 had highest number of cases; grade 1 showed a positivity percentage of 50% which was significantly higher than the positivity percentages of the higher grades.

In contrast to this Chaturvedi et al found 32.6% of positive cases in grade 3, 28.9% in grade 2 and the lowest percentages were found in grade 1 of around 23.5% indicating that they found more HER2/neu positive cases in the higher grades.

In Ivkovic et al the positive HER2/neu status meant a larger tumor of a higher grade with metastasis to the lymph nodes but the study by Chaturvedi et al (11,12) the tumors were of same size though they represented a higher grade furthermore they found that the HER2/neu negative tumors were of a lower grade. Our study showed similar findings as Ivkovic et al and Chaturvedi et al wherein they found HER2/neu negative status were much higher than the positive cases. (9,11)

It is well known fact that HER2/neu positivity does not bode well for the prognosis. (13-15) Seeing as most cases are diagnosed in higher grades, there are more cases of positivity in higher grades however the lower grades actually showed a higher percentage of HER2/neu positivity. Thus it would help to diagnose Breast carcinoma sooner, even in lower grades for better prognosis and therapeutic intervention.

Table 3: Comparative findings of Grade and HER2/neu findings in other studies compared to ours.

STUDIES	GRADE	Her2/neu status	
		Positive	Negative
Prati et al (N=130)	I	27	19
	II	36	26
	III	12	10
Chaturvedi et al (N=105)	I	4	13
	II	13	32
	III	14	29
Bouchbika et al	I+II	288	785
	III	147	262
Our Study (N=50)	I	2	2
	II	6	18
	III	2	20

CONCLUSION

Tabulating this data for the above findings yields a pattern which can be used as basis for future studies comparing the value of HER2/neu status. There appears to be a pattern whereby higher grades are having positive HER2/neu status however one must not rule out the fact that there are a good percentage of grade 1 tumors also that show HER2/neu positivity and one must not rule out the fact that most case of breast carcinoma that are diagnosed are grade 2 and above. Thus it would be really helpful to diagnose Breast carcinomas sooner as even lower grades may show HER2/neu positivity and thus poor prognosis.

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