ORIGINAL ARTICLE

IMMUNOHISTOCHEMICAL PROFILE OF BREAST CARCINOMAS IN CORRELATION WITH HISTOLOGICAL GRADE- EXPERIENCE OF A TERTIARY CARE HOSPITAL IN ANDHRA PRADESH

Aparna Chinnam[1], Swetha Naidu[2], Himabindu Gurram[3], Padmavathi Devi Chaganti[4]

Author's Affiliations: [1]Associate Professor; [2]Postgraduate; [3]Senior Resident; [4]Professor & Head, Dept. of Pathology, Guntur Medical College, Guntur, Andhra Pradesh, India.
Correspondence: Dr Aparna Chinnam Email: achinnam893@gmail.com

ABSTRACT

Background: Breast cancer is the most common female cancer worldwide. The two most important prognostic factors are histological grading(NBR Grading) and hormone receptor status namely estrogen receptor(ER)progesterone receptor(PR)and HER2. However few studies have evaluated the relationship between these two variables.

Aim: Aim of the present study was to correlate hormone receptor status with NBR Grading.

Material and methods: Breast cancer statistics were retrieved from the department records from 2012 to 2015.

Results: A total of 202 cases were subjected to immuno histochemistry Out of this 168 cases were stained for ER,PR and 34 cases for ER,PR and HER2. Out of this 66 cases were ER,PR positive, ER,PR negative were102 cases, triple positive were 20 cases, triple negative were14 cases, ER positive , PR negative were 20 cases, ER negative, PR positive were14.

Conclusion: There was not much correlation found between receptor status and grade of the tumor.

Keywords: Estrogen receptor, Progesterone receptor,HER-2 receptor ,triple positive, triple negative, NBR grading.

INTRODUCTION

Breast cancer is heterogenous disease. [1]It is the second most common cancer among women in India, after cancer cervix[2]. The information on the epidemiology of breast cancer is limited. Presently 75,000 new cases occur in Indian women every year.[3] Prognosis of breast cancer depends on more than 40 variables like age at presentation, size of the tumour, hormone receptor positivity, histological grade etc[4] but hormone receptor status plays a prime role in treatment as estrogen receptor positive tumors respond well to tamoxifen therapy and HER-2 positive cases to trastuzumab. ER is a nuclear transcription factor, that when activated by estrogen stimulates the proliferation of cells. PR also present on the nucleus, the presence of PR indicates that ER pathway is functional. HER-2 is present on chromosome 17. It encodes a growth factor receptor on cell membrane.[5] Aim of the present study was to correlate hormone receptor status with NBR Grading.

MATERIAL AND METHODS

Breast cancer statistics were collected from 1-8-2012 to 31-8-2015.All the cases were subjected to IHC. Formalin fixed paraffin processed tissues were routinely stained with Haematoxylin and Eosin. Later they were subjected to IHC for ER, PR, HER-2 using Dako antibodies.

RESULTS

Out of 202 cases 167 cases were reported as invasive duct cell carcinoma. out of 202 cases In situ duct cell carcinomas were 2, mucinous carcinomas

were seven, invasive papillary carcinomas were 6 cases, invasive lobular carcinoma one case, comedo carcinoma 2,medullary carcinomas were 2, signet ring cell one case, metaplastic carcinoma five cases, secretory carcinoma one case,pagets disease one case, and tumors with mixed pattern were 8 cases.

Table 1: The statistics of various morphological types of breast carcinomas

Type	Cases	ER +ve
In situ duct cell carcinoma	2	none
Invasive duct cell carcinoma	166	86
Invasive lobular carcinoma	1	1
Invasive papillary carcinoma	6	4
Medullary carcinoma	2	none
Mucinous carcinoma	7	7
Metaplastic carcinoma	5	1
Comedo carcinoma	2	1
Mixed patterns	8	3
Paget disease	1	none
Secretory carcinoma	1	1
Signet ring cell carcinoma	1	1

Out of 202 cases 66 cases ER, PR positive, 102 cases were ER,PR negative, HER-2 was done for 34cases. ER,PR,HER-2 were positive in 20 cases, negative in 14 cases, ER negative, PR positive in 14 cases, ER positive, PR negative in 20 cases.

Table 2: IHC profile of breast carcinomas

IHC	No.of cases
ER,PR +ve	66
ER,PR-ve	102
Triple +ve	20
Triple-ve	14
ER+ve,PR-ve	20
ER-ve,PR+ve	14

Out of 167 cases of invasive carcinoma no special type (NST) 112 cases were given NBR grade. Out of 31 cases of grade 1, only 16 cases were ER +ve, out of 72 cases of grade 2, 31 cases were ER +ve, out of 9 cases of grade 3 only 2 cases were ER+ve.

Table3: The statistics of ER positivity according to NBR grade

Grade	Total	Er+ve	Er-ve
Grade 1	31	16	15
Grade 2	72	31	41
Grade 3	9	2	7

DISCUSSION

Breast cancer is a heterogenous disease. Mortality rates depend upon a number of parameters; the two important parameters are histological grade of the tumor and hormone receptor status. Histological grade is done by Nottingham modification of Bloom- Richardson system. In this scheme, the grade is obtained by adding up the scores for tubule formation, nuclear pleomorphism and mitotic activity, each of which is given 1,2 or 3 points. This is translated into the final grade as 3-5 points is grade 1, 6-7 points is grade 2, 8-9 points as grade 3. In the present study out of 202 cases 167 cases (82%) were invasive duct cell carcinoma no special type (NST). [6] Out of this 112 cases were graded. 27% cases were grade 1,64.2% cases were of grade 2, only 8% were grade 3.[7]

Three molecular biomarkers are used in the routine management of breast cancer, those are ER, PR and HER2. Estrogen receptor is a nuclear transcription factor that, when activated by estrogen stimulates the growth of normal breast epithelial cells .Proliferation may also be activated in the cells of invasive breast carcinoma expressing ER which is detrimental. ER expression has been measured in invasive breast cancers by various methods for almost 40 years. But today IHC is the widely used method, which is sensitive, specific, easy, inexpensive, can be done on formalin fixed paraffin processed tissues. PR also routinely assessed by IHC in invasive breast cancers. ER regulates the expression of PR, presence of PR indicates that ER pathway is functional. PR is activated by progesterone which stimulates the growth of tumor cells. Four possible phenotypes are observed.[5]

1. ER+ve and PR+ve;
2. ER-ve and PR –ve;
3. ER-ve and PR+ve;
4. ER+ve andPr-ve.

There has been a lot of controversy whether ER-ve, PR +ve entity exists at all. For ER positive cases after treating with tamoxifen and aromatase inhibitors survival is more.

HER2/neu; is located on chromosome 17, encodes a growth factor receptor on the surface of normal breast epithelial cells. Gene amplified in 15% of tumor cells. HER2 positive cancers respond positively to targeted therapy with trastuzumab and lapatinib. Positive results are interpreted as 3+, characterized by strong, diffuse membrane staining (chicken wire) and 2+, at least 10% of cells showing complete membrane staining but weak intensity. Less than 10% of cells staining

and incomplete membrane staining are reported as negative.

According to the Ackerman, 80% of invasive duct cell carcinomas are positive for ER, but the prevalence of hormone positivity is low in Asian countries. [6] In the present study 42.5% are positive for ER. According to desai etal32.6% of tumors were ER+ve. In 'Fischer etal' study ER positive tumors have low grade histology, absence of tumor necrosis, marked tumor elastosis. In the present study in situ duct cell carcinomas were ER –ve, 51% of grade 1 tumors were ER +ve, 49% were ER –ve. But in grade 2 ,43% cases ER+ve, 57% ER –ve, in grade3, 22% are ER+ve, 78% are ER-ve.(table3) Low histological grade correlated with receptor positivity in Sepidae etal study.[8] In Desai etal study grade of the tumor correlated with hormone receptor status. [9]

American Society of Clinical Oncology (ASCO)/ College of American Pathologists (CAP) guidelines, for ER, PR IHC:

1. The pathologist must report the % of cells that are that are immuno reactive.
2. Tumors having 1% or more invasive cancer cell staining is regarded positive
3. The average intensity of the stain must be included.
4. The pathologist must give an interpretation as to whether stain is negative or positive.

The two main features that are evaluated are the proportion of stained cells and the intensity of staining. The first is expressed as the percentage of tumor nuclei population stained. There are several different methods to evaluate these parameters; Quick score, H score, Allred score.[10] In the present study Allred score is used.[(11)]

Allred score: The semi quantitation of this method is elegant yet simple. It incorporates intensity and proportion of nuclear staining for ER or PR. Add the proportion score (PS) and intensity score (IS) (PS+IS=TS) for the overall value of 0 to 8. [11]

ASCO guidelines for Her2 positivity[4]

1. IHC 3+ in >30% of invasive tumor cells;
2. FISH >6 HER2/neu nuclear copies;
3. FISH ratio of 2.2

Guidelines for negative result

1. IHC 0 or 1+;
2. FISH < 4 gene copies;
3. FISH ratio <1.8

CONCLUSION

In the present study ER positivity was low, in correlation with Indian literature. There is not much correlation with Histological grade and ER positivity. The study would have been better if disease free survival rates of the patients were also correlated with other parameters.

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