



The Histopathology of Carcinoma Breast with Special Reference to p53 Marker

Meera Balakrishnan^{1*}

¹Department of Pathology, Sree Balaji Medical College and Hospital, India.

Author's contribution

The sole author designed, analyzed, interpreted and prepared the manuscript.

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ABSTRACT

Introduction: Breast cancer is one of the most common cancers among women in the world. The high incidence of breast carcinoma in women has inspired a thorough investigation of potentially modifiable risk variables (clinical parameters, morphological type, and biochemical indicators) for prognosis, preventative tactics, and treatment options. One of the most important prognostic indicators for breast cancer is p53.

Aims and Objectives: The goal of this study was to use immunohistochemistry to assess the prevalence of p53 mutant protein in breast cancer, correlate the results with clinical and histological parameters, and establish its impact on axillary node metastasis.

Materials and Methods: A clinicopathological study of 50 cases of infiltrating ductal carcinoma of the breast was performed using immunohistochemistry to examine for p53 mutant protein expression.

Results: Percentage of p53 immunohistochemical positivity in this study was 22%, which is similar to other studies' reported statistics. In both the positive and negative cases of lymph node metastases, immunohistochemical data revealed an equivocal p53 status. In compared to p53 negative cases, the carcinomas with p53 positivity showed aggressive characteristics, such as greater size and higher grade. Patients with significant lymphocytic reactions to tumours, patients under 35 years of age, and those with tumours on the left side had a higher chance of receiving a positive p53 status. This study clearly shows that breast cancers with high p53 expression are generally aggressive tumours with a poor prognosis and a poor response to endocrine treatment and chemotherapy.

Keywords: Breast Cancer; p53; chemotherapy lymph node.

1. INTRODUCTION

Breast cancer one of the most widespread cancers in females and the leading cause of death in the Western world. Breast cancer is becoming more common in India and is approaching that of the Western world. Breast cancer is the second biggest cause of death among women in India, after carcinoma of the cervix. Carcinoma of breast accounts for 22% of all female cancers worldwide, 26% in affluent countries. The areas of high risk are affluent populations of North America, Europe, and Australia whereas areas of low risk are sub-Saharan Africa, Southern and Eastern Asia [1].

Breast being constantly under the influence of sex hormones, carcinoma of breast is associated with morbidity and mortality among woman of reproductive age group. This frequency of disease in woman has prompted intensive study risk factors (clinical parameters, morphological typing, and biological markers) in a developing breast cancer to gain clues to identify modifiable risk factor that would be helpful for assessment of prognosis, prevention strategies, and treatment modalities. Treatment of breast cancers is increasingly dependent on the biological phenotype of the tumours. Specific alterations call for specific types of therapy. For example, breast cancers expressing the estrogen receptor are highly responsive to Tamoxifen and those over-expressing the erbB2 oncoprotein are responsive to Herceptin [2].

The most common genetic event described so far in human cancer is a mutation in the p53 tumour suppressor gene. Normally, cells with wild type p53 can postpone the advancement of the cell cycle from the G1 to the S phase. During this time, aberrant DNA is repaired. When activated, the p53 protein is a DNA-binding protein that is located in the nucleus and controls the transcription of multiple other genes. Approximately 80% of the p53 point mutations found in human malignancies are found in the protein's DNA binding region. The mutated p53 protein is unable to bind to DNA and hence inhibits the action of the normal p53 protein. During the cell cycle, the normal p53 protein is called upon to apply emergency brakes [3,4].

An attempt is made to find out the association of p53 mutations among the 50 available cases of carcinoma breast using immunohistochemistry

and correlating the findings with clinical and histopathological parameters [5].

2. MATERIALS AND METHODS

80 cases diagnosed as carcinoma of breast on Hematoxylin and Eosin stained sections in the Department of Pathology, SreeBalaji Medical College and Hospital, Bharat University, during the period of April 2009 and September 2011 were included in the present study.

The biopsy material includes lumpectomy specimens, true cut biopsies and radical mastectomy specimens. The clinical details with reference to age and presenting complaint were recorded [Table 1].

The information was evaluated to determine the histological kinds of breast cancer, the type of clinical presentation, the age incidence, and the presence of p53 immuno-expression. The formalin-fixed, paraffin-embedded tumours were examined using hematoxylin and eosin-stained sections. The Nottingham composite histological grading method was used to determine the 80 cases of breast carcinomas. Each tumour was evaluated and scored numerically for the percent of tubule formation, the degree of nuclear pleomorphism, and the mitotic count in 10-high power fields using this grading system. To get an overall grade, the scores for each morphological characteristic were combined together. The size of the tumour, its grade, the presence of lymph nodes, and other prognostic factors were all documented and tabulated. Using the Super Sensitive Non-biotin HRP Detection System, 4-micron sections from 50 cases of paraffin blocks of breast tumours were subjected to immunohistochemistry examinations. The information gathered is linked. The results were compared to other workers' reports.

3. PROCEDURE

Four-micron thickness sections taken in poly-L-Lysine coated slides. They are allowed to dry 24 hours in room temperature. They are incubated in 60°C for 1hour in hot plate. The sections were deparaffinised with xylene for 15minutes each. The sections were hydrated through graded alcohols (100%, 95%, 90%, 70%) for 5 minutes each. Brought to running tap water for 10 minutes.

3.1 Antigen Retrieval

Citrate buffer with PH-6 were taken. Slides were immersed in it & boiled pressure cooker for 10 minutes. Allowed to cool to room temperature for 2 hours. Slides were washed in running tap water for 10minutes.

3.2 Staining Procedure

Slides were dipped in phosphate buffered saline (PBS) for 5 minutes. The slides were treated with 3% H₂O₂ for 5 minutes (to block endogenous peroxidase activity). Washed twice in PBS. The slides were incubated in 0.4% casein and washed in PBS for 5 minutes (to block protein cross reaction). Again incubated for 30 minutes with anti human p53 protein in room temperature. Washed in PBS.

3.3 Immunohistochemical Analysis of p53 Status⁵⁷

Positive p53 staining in any percentage of cancer cells was considered positive in our primary IHC study.

In a subsequent IHC examination, IHC-positive samples were divided into three categories based on the degree and extent of

immunostaining 58: P53 overexpression (p53+) was defined as dark nuclear staining of more than 10% of tumour cells, intermediate p53 overexpression (p53) was defined as mild nuclear staining of (1-10) percent of tumour cells, and the remaining group with less than 1% stained nuclei was defined as negative.

4. RESULTS

The final study comprised 50 patients who had been diagnosed with breast cancer. Breast cancers are distributed by age group, with specifics on tumour side and size. indicates the percentage of breast tumours that have spread to lymph nodes. An examination of numerous prognostic factors for breast malignancy. displays the percentage of p53 expression that is positive [Table 2] Association In this study, the relationship between age groups and outcome parameters is investigated. [Fig. 1] examines the relationship between tumor-related factors (side and size) and p 53 status. In 50 patients, the researchers looked at the link between lymph node metastases and p53 status. The relationship between p53 status and several prognostic indicators (tumour grading, Nottingham index, lymphocyte response, and necrosis) is investigated [Fig. 2,3].

Table 1. Age distribution of patients diagnosed with breast cancer

Age inyears	Numberof patients	%
31-40	22	27.5
41-50	43	53.8
51-60	12	15.0
>65	2	2.5
Total	80	100.0

Mean= ± SD. 45.28±7.51

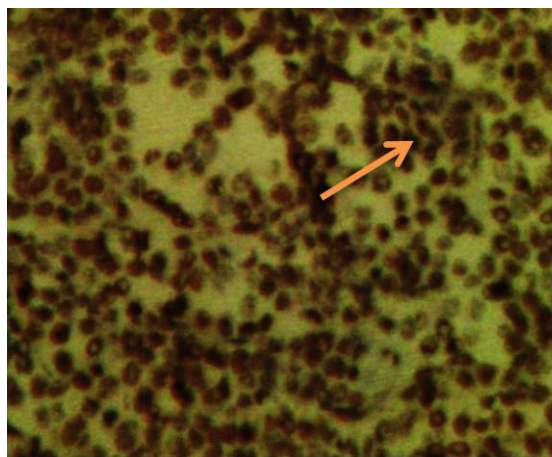


Fig. 1. IDC-NOS Histological grade III-p53 over expression (H&E x400)

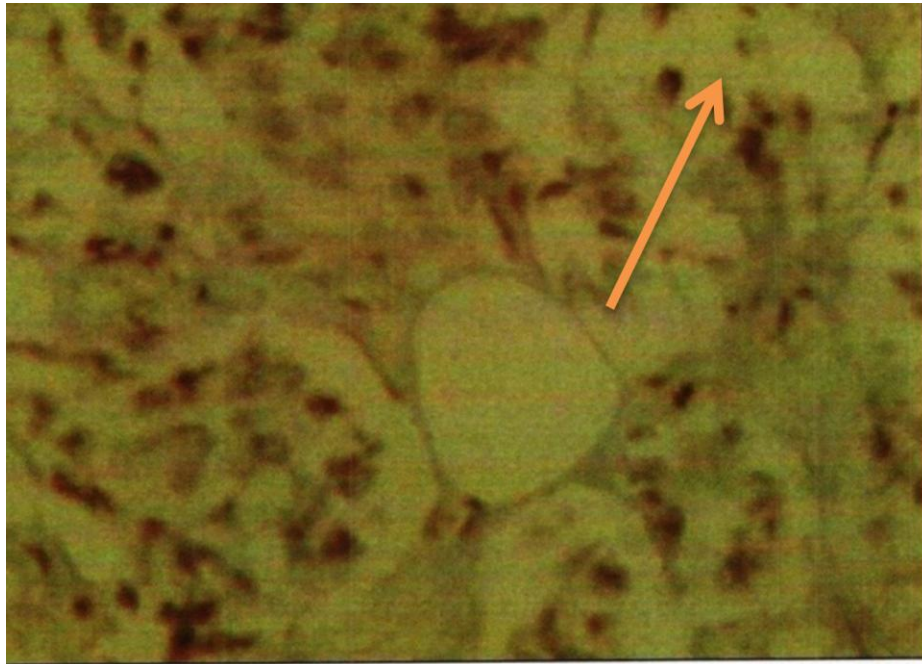


Fig. 2. IDC-NOS Histological grade II p53 weak expression (H&E x400)

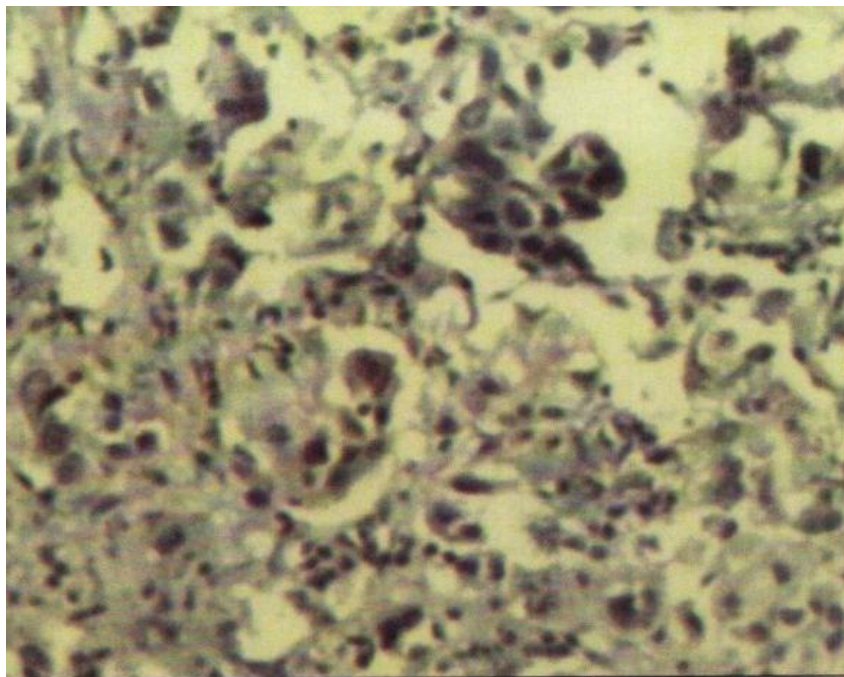


Fig. 3. IDC-NOS Histological grade II p53 negative (H&E x400)

Table 2. Association of p53 oncoprotein and tubular differentiation in breast carcinoma-SO cases

Tubular differentiation (TD)	n (%)>75% TD	n(o/o) (10-75)% TD	n (%,) <10% TD
p53 Positive (15)	1(7%)	13(86%)	1 (7%)
p53 Negative (35)	1(%)	29 (82%)	5 (14%)

5. DISCUSSION

Breast cancer is one of the most widespread tumours in women worldwide, accounting for nearly 22% of all cancers in women. Breast cancer is becoming more common in India and is approaching Western levels. Breast cancer has surpassed cervix cancer as the most frequent cancer in women, according to many population-based cancer registry statistics from India. This cancer is responsible for 19-34% of all cancer cases among women in the United States [6].

80 cases were studied out of which a clinico-pathological and immunohistochemical study was done for 50 cases. The data of those 50 cases were analyzed and compared with other workers.

In the present study, the youngest patient was 26 years and the eldest was 71 years. [Mean age - 45.28 years, Median age - 50 years]. The highest incidence of breast carcinoma was identified in the fifth decade, which was consistent with National Cancer Registry data [7,8].

Patients with p53 overexpressing tumours were slightly younger on average than those without p53 overexpressing tumours in our study [9,10].

6. CONCLUSION

This study clearly shows that breast cancers with high p53 expression are generally aggressive tumours with a poor prognosis and a poor response to endocrine treatment and chemotherapy.

CONSENT AND ETHICAL APPROVAL

As per international standard or university standard guideline Patient's consent and ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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