

Elastosis in premalignant and malignant lesions of breast-A histopathological and histochemical study

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Abstract

Background: Stromal changes in all the premalignant, insitu/ microinvasive and invasive malignant lesions of breast helps in better understanding of disease process at the level of the tumor and host stromal reaction. The pattern of elastosis even correlates better with prognosis than the predicted behaviour of tumour cells. **Aims and Objectives:** The present study is undertaken to emphasize the importance of stromal changes (elastosis) and to predict the prognosis and behaviour of tumor cells. **Study design:** The study was conducted on 90 patients of breast lesions (66 cases of invasive malignant breast lesions and 04 cases of insitu breast lesions and 20 cases of proliferative breast lesions). **Material and Methods:** The tissue for histopathological studies were collected in 10 % buffered formalin solution .The paraffin wax blocks were made and 4-5 μ thick sections were cut and stained by H & E and special histochemical stains. **Result:** Moderate degree of elastosis was found to be associated with maximum number of invasive malignant breast lesions Proliferative breast lesions and insitu malignant lesions showed mild to moderate degree of elastosis. Consistent results were obtained in Grade II malignant lesion where moderate to marked degree of elastosis was seen. **Conclusion:** In all cases of early invasive and invasive malignant lesions of breast, elastosis as a indicator of stromal change should be carefully studied and included in predicting the final outcome along with histological types to get the better results.

Key words: Breast, Stroma, Malignant, Elastosis

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Introduction

Reciprocal interaction between epithelium and mesenchyme mediates crucial aspects of embryonic development and direct the coordinated organogenesis correct spatial orientation and timely expression of functional activity consistent with physiological demands. In carcinomas, the cellular organization is dramatically changed and the stroma is extensively modified .The basement membrane is penetrated in a process of degradation and /or decreased synthesis and the surrounding stroma results in neovascularisation , inflammatory cell influx , sarcoid like granulomatous reaction and extensive remodelling of extracellular matrix in the form of fibrosis and elastosis. A prominent feature of stromal reaction in most breast cancers is the presence of elastic tissue element, a process called

elastosis [1]. The presence of elastosis or elastic tissue in the stroma of sections from breast carcinoma was first described by Cheatele and Cutler [1].

It has been found that while fibroblastic cells of the stroma and of the periductal region are responsible for elastin synthesis in most breast cancers, the malignant epithelium is a source of the elastin in the desmoplastic tissue of a significant proportion of such neoplasm [2].

The tumour stroma in breast has been neglected in many studies. Upcoming prevention, diagnostic and therapy strategies and studies should be carried out in an unbiased way, allowing analyses of the stromal compartment in addition to the classical investigations of the epithelial cancer component [3].

Importance of stroma in breast cancer has been highlighted in several studies [4].

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Benign conditions such as fibroadenoma and sclerosing adenosis produced no significant elastosis [5,6]. There is a correlation between elastosis and estrogen receptor expression as well as response to antihormonal therapy [7]. During tumor development, reciprocal signalling patterns between the cancer cells and the surrounding tissue are altered in a way that affects tissue architecture and cell fate [8].

In addition, a recent study classifying tumour stroma found that collagen and fibroblast dominant groups were associated with poor outcome [9]. Demonstration of elastosis in premalignant lesions and in the early invasive stages of breast carcinoma, where the doubtful diagnosis exists with the help of histochemical stains and few newer technique like histoenzymology can be very useful features, beside this prognosis of some tumours can also be predicted as well. Various studies demonstrate that stromal morphologic structure as a previously unrecognized prognostic determinant for breast cancer [10]. High elastosis content associated

with clinicopathological characteristics of good prognosis and low tumour cell proliferation ki67 [11].

The present study is undertaken to emphasize the importance of elastosis as stromal change and to predict the prognosis and behaviour of tumor cells.

Materials and Methods

The study was a retrospective and prospective study for a period of three years from November 2012 to October 2015 and conducted on 90 patients of breast lesions (66 cases of invasive malignant breast lesions and 04 cases of insitu breast lesions and 20 cases of proliferative breast lesions) conducted in the department of pathology L. N Medical college and associated J. K. Hospital Bhopal.

The tissue for histopathological studies were collected in 10 % buffered formalin's. The paraffin wax blocks were made and 4-5 μ thick sections were cut and stained by H & E and special histochemical stains i.e Verhoffs stain

Results

Table No 1: Relationship between degree of elastosis and tumor type;

Table below shows that moderate degree of elastosis (70%) was seen in invasive ductal carcinoma (NOS), while absent to slight elastosis was seen only in medullary and colloid carcinoma.

Degree of elastosis	Tumor type					
	Intraductal /microinvasive ca	Invasive ductal ca (NOS)	Medullar ca	Colloid ca	Tubular ca	Lobular carcinoma
Absent	-	-	01 (1.43%)	01 (1.43%)	-	-
Slight	03 (4.28%)	02 (2.86%)	01 (1.43%)	-	-	-
Moderate	01 (1.43%)	49 (70%)	-	-	01(1.43%)	02 (2.86%)
Marked	-	09 (12.8%)	-	-	-	-
Total	04 (5.71%)	60 (85.7%)	02 (2.86%)	01(1.43%)	01(1.43%)	02 (2.86%)

Table No 2: Relationship of elastosis with histological grading (modified Bloom Richardson's grading, 1991) among 66 invasive tumors.

Table below reveals that moderate degree of elastosis was seen in most of the cases with Grade II tumours revealing around 72.7% of moderate degree of elastosis.

Degree of elastosis	Grade I	Grade II	Grade III
Absent	-	-	01(1.5%)
Slight	03 (4.54%)	01(1.5%)	01(1.5%)
Moderate	03(4.54%)	48(72.7%)	-
Marked	-	06(9.09%)	03(4.54%)
Total	06(9.09%)	55(83.3%)	05(7.5%)

Table No 3: Relationship of degree of elastosis with proliferative breast lesions.

Table below reveals that severity of elastosis increased with the severity of disease.

Proliferative breast lesions (20)	Degree of elastosis	Degree of epitheliosis/Severity of lesion
16 (80%)	Mild	Mild to moderate degree of epitheliosis
04 (20%)	Moderate	Severe degree of epitheliosis
Total- 20	-	-

Discussion

The present study revealed that the incidence of elastosis in carcinoma breast found to be > 90%. Consecutive sections were stained by Mayers Hemalum and eosin for general observational microscopy

Moderate degree of elastosis was found to be associated with maximum number (70%) of cases -According to a study as illustrated in the paper by Shivas and Douglas they classified the degree of elastosis on the four point scale 0-4; 0 indicated no elastosis and 1-3 indicated increasing amount of elastosis i.e. mild, moderate and severe degree of elastosis [14]. On correlating the degree of elastosis with histological types maximum number of cases of IDC (NOS) showed moderate to marked degree of elastosis, while medullary carcinoma and mucinous (colloid) carcinoma showed absent/ slight degree of elastosis. Elastosis was correlated with histological grades (modified Bloom Richardson grade 1991). Elastosis was correlated with histological grades in which moderate to marked degree of elastosis was seen in grade II tumours. Fisher et al (1975) [12] also found consistent associations with only marked and moderate degree of elastosis with Grade II tumor.

Various patterns of elastosis in the form of periductal, perivascular, and stromal elastosis were seen. Periductal elastosis found not only around the ducts containing neoplastic cells but also around the ducts with atypical epithelial hyperplasia.

- 20 cases of Proliferative breast disease were studied which illustrated mild degree of elastosis was seen in most of the cases. Degree of elastosis increases with severity of disease ranging from mild to moderate degree.

- Parfrey NA 1985 also noted grades of periductal elastosis and stromal elastosis increase progressively with the severity of breast disease [6]. Desmoplasia and elastosis are kind of host cell reaction, produced by stromal tissue in response to the tumour cells. When

Toluidine blue stain was applied on sections, showing areas of Ca in situ, pink metachromasia is seen around the ducts where duct wall were damaged partially, while absent metachromasia is seen where the duct walls were completely intact.

Heartveit F (1981), found that these changes are preceded by mast cells degranulation [13]. Compared to normal tissue the stroma accompanying breast tumours contain an increased number of fibroblasts, immune cell infiltration, enhanced capillary density increased collagen and fibrin deposition [7]. In our study it is found that elastosis is a typical response in the breast to infiltrating duct and lobular carcinoma, with no significant differences between these two types in terms of the stromal response The elastic fibres present in normal breast have had a low microfibril: elastin ratio [4]. Breast cancer stromal elastosis is associated with mammography screening detection, low Ki67 expression and favourable prognosis in a population based study [10].

Limitations: Stromal response in the form of elastosis is seen in both ductal and lobular carcinoma, with no significant difference in the degree of elastosis, hence these two variants can't be differentiated on the basis of degree elastosis.

Conclusion

Recognition of the important role of the stroma during progression of the breast cancer leads to the possible identification of new targets for treatment of the initial breast cancer lesion as well as prevention of recurrence. In all cases of early invasive and invasive malignant lesions of breast, elastosis as a stromal change should be carefully studied and included in predicting the final outcome along with histological types to get the better results.

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