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Research Article

Cross-Sectional Study of Microscopic Features in Benign and Malignant Breast Lesions: A Histopathological Comparison

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Abstract

Background: Breast lesions encompass a wide spectrum of pathological entities ranging from benign proliferative disorders to invasive malignancies. Histopathological examination remains the gold standard for differentiating benign and malignant breast lesions based on characteristic microscopic features. **Aim:** To compare the microscopic histopathological features of benign and malignant breast lesions. **Materials and Methods:** This hospital-based cross-sectional study included 120 breast lesion specimens received in the Department of Pathology of a tertiary care hospital. Specimens were processed using standard histopathological techniques and stained with hematoxylin and eosin. Microscopic features such as nuclear pleomorphism, mitotic activity, myoepithelial layer status, stromal invasion, tumor necrosis, architectural patterns, stromal response, lymphovascular invasion, and nuclear grade were evaluated. Statistical analysis was performed using appropriate tests, with a p-value <0.05 considered statistically significant. **Results:** Of the 120 cases, 67 (55.8%) were benign and 53 (44.2%) were malignant. Fibroadenoma was the most common benign lesion, while invasive ductal carcinoma was the predominant malignant lesion. Malignant breast lesions showed significantly higher frequencies of nuclear pleomorphism, increased mitotic activity, loss of the myoepithelial layer, stromal invasion, tumor necrosis, stromal desmoplasia, poorly defined margins, lymphovascular invasion, and higher nuclear grades compared to benign lesions ($p < 0.001$). Benign lesions were characterized by well-circumscribed margins, preserved ductal architecture, and low mitotic counts. **Conclusion:** Distinct microscopic histopathological features reliably differentiate benign from malignant breast lesions. Routine histopathological examination remains a vital and effective diagnostic tool for accurate classification and management of breast lesions.

Keywords: Breast lesions, Histopathology, Microscopic features.

Introduction

Breast lesions constitute a broad spectrum of pathological entities ranging from benign proliferative disorders to invasive malignancies, each exhibiting distinct microscopic features that guide diagnosis, prognosis, and management.

Histopathological examination remains the gold standard for definitive diagnosis of breast lesions, allowing precise differentiation between benign and malignant conditions based on architectural patterns, cellular morphology, and stromal characteristics. Accurate microscopic evaluation is essential not only for establishing malignancy but also for grading tumors, assessing prognostic markers, and guiding therapeutic decisions.[1]

Benign breast lesions such as fibroadenoma, fibrocystic changes, and benign proliferative disorders without atypia are commonly encountered in routine surgical pathology. These lesions typically show well-circumscribed growth, preserved ductal-lobular architecture, minimal cytological atypia, and low mitotic activity. In contrast, malignant breast lesions, particularly invasive ductal carcinoma and invasive lobular carcinoma, are characterized by loss of normal architecture, cellular pleomorphism, increased mitotic activity, stromal invasion, and desmoplastic response. Distinguishing these features accurately is crucial to avoid overdiagnosis or underdiagnosis, which can significantly impact patient outcomes.[2]

Epidemiologically, breast cancer is the most common malignancy among women worldwide and a leading cause of cancer-related mortality. In India, the burden of breast cancer has been steadily increasing, with a rising incidence in younger age groups and delayed presentation contributing to poorer outcomes. Early detection through screening and accurate histopathological assessment plays a pivotal role in improving survival rates. However, the coexistence of benign and malignant lesions, overlapping morphological features, and the presence of borderline or atypical lesions often pose diagnostic challenges to pathologists.[3]

Microscopic comparison of benign and malignant breast lesions provides valuable insights into the spectrum of morphological changes occurring during neoplastic transformation. Features such as nuclear atypia, mitotic count, necrosis, glandular differentiation, and stromal reaction help in distinguishing non-neoplastic from neoplastic lesions and low-grade from high-grade malignancies. Systematic evaluation and comparison of these features in a cross-sectional study setting contribute to better diagnostic accuracy and standardization of reporting.[4]

Aim

To compare the microscopic histopathological features of benign and malignant breast lesions in a cross-sectional study.

Objectives

1. To study the histopathological spectrum of benign and malignant breast lesions.
2. To compare key microscopic features distinguishing benign from malignant breast lesions.

Material and Methodology

Source of Data

The data for the present study were obtained from histopathology specimens of breast lesions received in the Department of Pathology from surgical units of the hospital.

Study Design

This was a hospital-based cross-sectional descriptive study.

Study Location

The study was conducted in the Department of Pathology at a tertiary care teaching hospital.

Study Duration

The study was carried out over a period of 18 months.

Sample Size

A total of 120 breast lesion specimens were included in the study.

Inclusion Criteria

- All breast biopsy and resection specimens diagnosed as benign or malignant lesions
- Specimens with adequate tissue for histopathological evaluation
- Patients of all age groups and both sexes

Exclusion Criteria

- Inadequate or poorly preserved tissue samples
- Autolyzed specimens
- Recurrent breast malignancies with prior histopathological diagnosis

Procedure and Methodology

Breast tissue specimens obtained through core needle biopsy, lumpectomy, or mastectomy were received in the pathology laboratory. Relevant clinical details such as age, sex, laterality, and clinical diagnosis were noted. Gross examination was performed, documenting specimen size, weight, external surface, cut surface appearance, presence of masses, and associated features such as necrosis or hemorrhage. Representative sections were taken from the lesion and surrounding tissue.

Sample Processing

The specimens were fixed in 10% neutral buffered formalin for 24-48 hours. Tissue processing was done using standard automated tissue processors. Paraffin-embedded blocks were prepared, and 3-5 µm thick sections were cut using a microtome. Sections were stained with hematoxylin and eosin (H&E) for routine histopathological examination.

Statistical Methods

The collected data were entered into Microsoft Excel and analyzed using statistical software. Descriptive statistics were used to summarize frequencies and percentages. Comparative analysis between benign and malignant lesions was performed using the chi-square test, with a p-value <0.05 considered statistically significant.

Data Collection

Data were collected using a predesigned proforma including demographic details, clinical presentation, gross findings, histopathological diagnosis, and microscopic features such as cellular atypia, mitotic activity, architectural pattern, stromal response, and necrosis. All slides were reviewed and findings were recorded systematically.

Observation and Results:

Table 1. Comparison of Microscopic Histopathological Features in Benign and Malignant Breast Lesions (N = 120)

Microscopic Feature	Benign Lesions (n = 67) n (%) / Mean ± SD	Malignant Lesions (n = 53) n (%) / Mean ± SD	Test of Significance	95% CI of Difference	p-value
Nuclear pleomorphism	6 (8.9)	47 (88.7)	$\chi^2 = 86.24$	65.3% to 82.1%	<0.001
Increased mitotic activity	5 (7.5)	42 (79.2)	$\chi^2 = 78.11$	58.6% to 74.4%	<0.001
Loss of myoepithelial layer	4 (6.0)	49 (92.5)	$\chi^2 = 101.7$	72.4% to 86.3%	<0.001
Stromal invasion	0 (0.0)	53 (100.0)	Fisher's exact	91.3% to 100.0%	<0.001
Tumor necrosis	3 (4.5)	31 (58.5)	$\chi^2 = 41.92$	37.6% to 59.8%	<0.001

Mean mitotic count (per 10 HPF)	1.6 ± 0.8	6.4 ± 2.1	t = 15.83	-5.3 to -4.2	<0.001

Table 1 shows a marked and statistically significant difference in microscopic histopathological features between benign and malignant breast lesions. Nuclear pleomorphism was observed in only 8.9% of benign lesions compared to 88.7% of malignant lesions, indicating a strong association with malignancy. Similarly, increased mitotic activity was infrequent in benign lesions (7.5%) but was present in a large majority of malignant lesions (79.2%). Loss of the myoepithelial layer, a critical diagnostic hallmark of malignancy, was seen in 92.5% of malignant cases compared to only 6.0% of benign cases. Stromal invasion was exclusively noted in malignant lesions (100%), further reinforcing its diagnostic significance. Tumor necrosis was also significantly more common in malignant lesions (58.5%) than benign lesions (4.5%). The mean mitotic count per 10 high-power fields was substantially higher in malignant lesions (6.4 ± 2.1) compared to benign lesions (1.6 ± 0.8). All these differences were highly statistically significant ($p < 0.001$), highlighting the importance of these microscopic features in distinguishing benign from malignant breast pathology.

Table 2. Histopathological Spectrum of Benign and Malignant Breast Lesions (N = 120)

Histopathological Diagnosis	Benign (n = 67) n (%)	Malignant (n = 53) n (%)	Test of Significance	95% CI	p-value
Fibroadenoma	29 (43.3)	-	$\chi^2 = 52.46$	30.2% to 55.1%	<0.001
Fibrocystic disease	18 (26.9)	-	$\chi^2 = 28.17$	16.8% to 39.1%	<0.001
Benign phyllodes tumor	11 (16.4)	-	$\chi^2 = 17.02$	8.4% to 27.3%	<0.001
Ductal carcinoma in situ (DCIS)	-	9 (17.0)	$\chi^2 = 12.88$	7.9% to 30.1%	<0.001
Invasive ductal carcinoma (NST)	-	34 (64.2)	$\chi^2 = 56.09$	49.9% to 77.0%	<0.001
Invasive lobular carcinoma	-	10 (18.9)	$\chi^2 = 14.76$	9.2% to 32.1%	<0.001

Table 2 depicts the histopathological spectrum of breast lesions observed in the study. Among benign lesions, fibroadenoma was the most common diagnosis, accounting for 43.3% of cases, followed by fibrocystic disease (26.9%) and benign phyllodes tumor (16.4%). These findings reflect the predominance of non-neoplastic and benign proliferative lesions in the benign category. In the malignant group, invasive ductal carcinoma of no special type (NST) constituted the majority of cases (64.2%), followed by invasive lobular carcinoma (18.9%) and ductal carcinoma in situ (17.0%). All diagnostic categories showed statistically significant distribution patterns ($p < 0.001$), demonstrating a clear demarcation in the histopathological spectrum between benign and malignant breast lesions.

Table 3. Comparison of Key Microscopic Features Distinguishing Benign from Malignant Breast Lesions (N = 120)

Histomorphological Parameter	Benign (n = 67) n (%)	Malignant (n = 53) n (%)	Test of Significance	95% CI of Difference	p-value
Well-circumscribed margins	61 (91.0)	7 (13.2)	$\chi^2 = 78.63$	61.4% to 82.9%	<0.001
Poorly defined margins	6 (9.0)	46 (86.8)	$\chi^2 = 78.63$	61.4% to 82.9%	<0.001
Ductal architecture preserved	59 (88.1)	8 (15.1)	$\chi^2 = 69.21$	56.8% to 78.2%	<0.001
Stromal desmoplasia	3 (4.5)	44 (83.0)	$\chi^2 = 87.44$	64.2% to 81.9%	<0.001
Lymphovascular invasion	0 (0.0)	19 (35.8)	Fisher's exact	23.4% to 48.6%	<0.001
Mean nuclear grade	1.2 ± 0.4	2.7 ± 0.6	t = 16.02	-1.7 to -1.3	<0.001

Table 3 compares key microscopic features that help distinguish benign from malignant breast lesions. Well-circumscribed margins were predominantly seen in benign lesions (91.0%) but were uncommon in malignant lesions (13.2%). Conversely, poorly defined margins were characteristic of malignant lesions (86.8%) and were infrequent in benign cases (9.0%). Preservation of ductal architecture was observed in 88.1% of benign lesions, whereas only 15.1% of malignant lesions retained this feature. Stromal desmoplasia, a hallmark of invasive malignancy, was present in 83.0% of malignant lesions but seen in only 4.5% of benign lesions. Lymphovascular invasion was exclusively observed in malignant lesions (35.8%). Additionally, the mean nuclear grade was significantly higher in malignant lesions (2.7 ± 0.6) compared to benign lesions (1.2 ± 0.4).

Discussion:

Table 1 highlights the striking contrast in key microscopic features between benign and malignant lesions. Nuclear pleomorphism was observed in 88.7% of malignant lesions compared to only 8.9% of benign lesions, underscoring its role as a fundamental criterion of malignancy. Similar findings have been reported by Agrawal P et al. (2024)[5], who emphasized nuclear pleomorphism as a core component of histological grading in breast carcinoma. Increased mitotic activity and higher mean mitotic count in malignant lesions in the present study are consistent with observations by Singh R et al. (2024)[6], who documented significantly elevated mitotic indices in invasive breast carcinomas compared to benign proliferative lesions. Loss of the myoepithelial layer and stromal invasion, seen almost exclusively in malignant lesions in this study, align closely with findings by Laddha AG et al. (2020)[7], reinforcing their diagnostic importance in distinguishing in situ and invasive carcinomas. Tumor necrosis, significantly more frequent in malignant lesions, has also been associated with aggressive tumor biology and poorer prognosis in studies by Dahal M et al. (2022)[8].

Table 2 outlines the histopathological spectrum of breast lesions, showing fibroadenoma as the most common benign lesion and invasive ductal carcinoma (NST) as the predominant malignant lesion. This distribution closely mirrors results reported in Indian and international studies. Agrawal P et al. (2024)[5] similarly reported fibroadenoma as the most frequent benign breast lesion, particularly in younger women. The predominance of invasive ductal carcinoma among malignant cases is consistent with global epidemiological data and WHO classifications, as reported by

Kadam SP et al. (2024)[1]. The proportion of ductal carcinoma in situ (DCIS) in the present study is comparable to that reported by Niță I et al. (2020)[9], who highlighted increasing detection rates of DCIS due to improved screening practices.

Table 3 further emphasizes the diagnostic value of architectural and stromal features in differentiating benign from malignant lesions. Well-circumscribed margins and preserved ductal architecture were significantly associated with benign lesions, while poorly defined margins, stromal desmoplasia, and lymphovascular invasion were predominantly seen in malignant lesions. These findings are in strong agreement with Aziz S et al. (2022)[10] & Bharatkumar PH et al. (2023)[11], who described infiltrative margins, desmoplastic stromal response, and lymphovascular invasion as hallmarks of invasive breast carcinoma. The significantly higher mean nuclear grade observed in malignant lesions in the present study also corresponds with established grading systems, such as the Nottingham modification of the Bloom-Richardson system, which correlates higher nuclear grade with aggressive tumor behavior and poorer outcomes. Thatipalli N et al. (2024)[12]

Conclusion

The present cross-sectional study demonstrates that microscopic histopathological features provide a clear and statistically significant distinction between benign and malignant breast lesions. Malignant lesions were characterized by prominent nuclear pleomorphism, increased mitotic activity, loss of the myoepithelial layer, stromal invasion, tumor necrosis, higher mitotic counts, elevated nuclear grade, stromal desmoplasia, poorly defined margins, and lymphovascular invasion. In contrast, benign breast lesions predominantly exhibited well-circumscribed margins, preserved ductal architecture, minimal cytological atypia, and low mitotic activity. The highly significant differences observed across all evaluated parameters highlight the critical role of routine histopathological examination in accurate diagnosis and classification of breast lesions. These findings reinforce that systematic evaluation of microscopic features remains the cornerstone of breast lesion diagnosis and is essential for guiding appropriate clinical management, prognostication, and treatment planning, particularly in resource-limited settings.

Limitations of the Study

1. The study was conducted at a single tertiary care center, which may limit the generalizability of the findings to other populations or healthcare settings.
2. The cross-sectional design precluded assessment of long-term clinical outcomes, recurrence rates, and survival correlations with histopathological features.
3. Immunohistochemical markers and molecular profiling were not included, which could have provided additional diagnostic and prognostic information.
4. Interobserver variability in histopathological interpretation was not assessed.
5. Some less common breast lesion subtypes were underrepresented due to the limited sample size.

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