



**RARE HISTOPATHOLOGICAL LESIONS OF THE BREAST-4- YEAR STUDY IN  
A TERTIARY CARE HOSPITAL**

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**ABSTRACT**

A wide spectrum of benign and malignant lesions may involve the breast. Many of these lesions are rare. These lesions may be encountered upon the histopathological examination of breast biopsies and specimens. Many of these lesions benign as well as malignant may mimic each other on microscopic examination. A pathologist should be well familiar with all these rare entities to arrive at a proper histopathological diagnosis for management. The purpose of the current study is to review rare cases of breast lesions along with histopathological features in the department of pathology over a period of four years.

**Key words:**

Rare lesions, breast, histopathology

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**INTRODUCTION**

A wide spectrum of benign and malignant lesions may involve the breast. Many of these lesions are rare. These lesions may be encountered upon the histopathological examination of breast biopsies and specimens. Many of these lesions benign as well as malignant may mimic each other on microscopic examination. A pathologist should be well familiar with all these rare entities to arrive at a proper histopathological diagnosis for management. The purpose of the current study is to review rare cases of breast lesions along with histopathological features in the department of pathology over a period of four years.

**METHODS**

The current study is retrospective in nature conducted in the department of pathology, Government Medical College, Srinagar, over a period of 4 years from January, 2014 to December, 2017. A total of 50 cases were included and studied. The specimens included were core biopsies, excision biopsies and resected specimens. All the required details were retrieved from the department based records and the corresponding H&E stained slides were collected from the departmental archival material and were reviewed. All the cases were analyzed regarding age, gender and prominent histopathological morphology.

**RESULTS**

All the 50 cases included in our study were neoplastic lesions- benign and malignant.

The benign ones included the lesions like benign phyllodes, intraductal papilloma, tubular adenoma, lipoma, neurofibroma and leiomyoma. The malignant ones included the lesions like malignant phyllodes, invasive lobular carcinoma, medullary carcinoma of breast, metaplastic carcinoma including squamous cell carcinoma, inflammatory carcinoma, neuroendocrine carcinoma, paget's disease, lymphoma, and fibrosarcoma. (Table 1)

Benign phyllodes were found in young females in the age range of 25 to 40 years at presentation. At histopathological analysis, the sections showed both epithelial and stromal components, the bilayer of epithelial and myoepithelial cells in most of the lesions. The stroma showed mild, moderate to marked cellularity in different lesions comprising of mostly plump spindle cells with only mild atypia and few mitosis (<5 per 10 high power field) in some of the lesions. Occasional bizarre cells were seen in one of the lesions but other features of malignant phyllodes were absent. All the lesions typically had smooth and non infiltrative borders.

A single case of malignant phyllodes was seen in a 48 year old Female. It involved the left breast. On histological analyses, stromal cells showed marked nuclear pleomorphism and overgrowth, mitosis  $\geq$  10per High power field. Sarcomatous elements were not identified.

About 6 cases of tubular adenoma were seen in young females with age group in the range of 16 -28 years. Ductal adenoma was seen in a female aged 38 years old. On histopathology, typical intra ductal proliferation of glands with epithelial and myoepithelial linings were seen.

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Intraductal papilloma was seen in 4 cases belonging to age group in the range of 25 to 46 years. All the 4 lesions were central papillomas. Histology of the lesions showed fibrovascular cores lined by myoepithelial cells with overlying epithelial cells. Areas of hemorrhage, fibrosis and foci of calcification were seen in some lesions.

About 6 cases of Lipoma were seen in females in age range of 36 to 45 years. Histopathological examination showed sheets of mature adipocytes with eccentric nuclei.

2 cases of neurofibroma were seen, one was a 40 year old and another 52 year old female. Histopathological examination revealed a spindle cell lesion with cells arranged in storiform pattern which were confirmed on IHC as neurofibroma.

2 cases of Paget's disease were seen. One was a 42 year old female presenting in left breast and another a 54 year old female with bilateral disease. Histopathological examination showed large clear cells with hyperchromatic nuclei and prominent nucleoli in epidermis and was associated with in situ carcinoma of the same breast in one of the cases.

There were 2 cases of leiomyoma one a 37 year old female and other a 2year old female showing typical features of leiomyoma. One of the cases showed benign spindle cells without any atypia and mitosis and the other showed mild atypia but mitotic count was not increased.

In our study, there was a single case of lymphoma over a period of 4 years found in a 50 year old female. It was a primary lymphoma of the breast. On microscopy, features were those of Diffuse Large B cell Lymphoma as was confirmed upon IHC.

In our study there were 4 cases of Invasive Lobular carcinoma that belonged to females with age >50 years. Sections showed cells with discohesive pattern of infiltration with oval nuclei, small amount of cytoplasm and intracytoplasmic lumina. One of cases showed features of solid variant of Invasive Lobular carcinoma. Foci of Lobular carcinoma in situ were seen in one of the cases.

A case of Fibrosarcoma in a 56 year old female presenting as a breast lump was identified. Microscopically the tumor showed spindle shaped cells arranged in herringbone pattern with collagenous stroma. Few mitotic figures were seen along with few giant cells.

There were 3 cases of medullary carcinoma seen in a 40, 42 and 38 year old female in our study. The tumor showed circumscribed margin with cells arranged syncytial growth pattern of the cells, vesicular nuclei, increased mitosis and inflammatory infiltrate.

Two cases of neuroendocrine carcinoma breast were identified in our study-a 45 year old and a 48 year old. Sections showed uniform cells, growing in solid nests, with eosinophilic cytoplasm and stippled chromatin. One of the cases showed high grade nuclear features. Both the cases showed positivity for neuroendocrine markers.

**Table 1** Spectrum of lesions of rare lesions of breast

S No.	Histopathological diagnosis	Nature of lesion	No. of Cases
1.	Benign Phyllodes		9
2.	Tubular adenoma		6
3.	Lipoma		6
4.	Intraductal papilloma	<b>Benign</b>	4

5.	Neurofibroma		2
6.	Leiomyoma		2
7.	Malignant Phyllodes		1
8.	Invasive Lobular carcinoma		4
9.	Medullary carcinoma		3
10.	Metaplastic carcinoma		5
11.	Inflammatory carcinoma		1
12.	Paget's disease		2
13.	Neuroendocrine carcinoma	<b>Malignant</b>	2
14.	Lymphoma		1
15.	Fibrosarcoma		1

## DISCUSSION

Phyllodes tumors are rare fibroepithelial lesions and make up 0.3 to 0.5 % of female breast tumors.<sup>2</sup> Most of the tumor arises in women aged between 35 and 55 years.<sup>2,4</sup> In our study, phyllodes tumor, both benign and malignant comprised only 0.02-0.03% of the tumors of the breast over the period of 4 years. Phyllodes tumor was found in females in the age range of 25 to 50 years. There was one case of malignant phyllodes in a 38 year old female. Jacobs *et al.* found that 4 stromal features i.e., cellularity, nuclear atypia, mitoses, and amount of stroma relative to epithelium differed significantly between cases that were fibroadenoma at excision compared with those that were phyllodes tumor. Among the subset of cases with moderate stromal cellularity, the presence of stromal mitoses remained the single histological feature significantly different between the phyllodes tumor and fibroadenoma.<sup>5</sup>

Tubular adenoma is a rare benign epithelial tumor of the breast accounting for 0.13 - 1.7% of benign breast lesions.<sup>6</sup> In our study there were around 1.2 % cases of tubular adenoma. Tubular breast adenomas most often affect young women of reproductive age<sup>7</sup> and have not been associated with oral contraceptive treatment or pregnancy.<sup>6</sup> In 90% of the cases these tumors are found in patients younger than 40 years. Microscopy shows the tumor is characterized by the presence of tightly packed homogenous tubular and acinar epithelial components with sparse intervening stroma on contrary to fibroadenoma which contains a large amount of stroma.<sup>7</sup> Tubular lumens are small and empty but sometimes may contain eosinophilic proteinaceous material. Focal of extensive infarction has been reported in some.<sup>8</sup> Almost all the cases in our study revealed small tubular structures in loosely vascularized cellular but sparse stroma. Eosinophilic proteinaceous material was seen in two cases.

Intraductal Papilloma is a benign tumor found within breast ducts. Intraductal papilloma can occur in women of all ages but most commonly between 35-55 years of age.<sup>9</sup> Intraductal papilloma makes up less than 10% of benign breast lesions and less than 1% of malignant breast tumors.<sup>10</sup> In our study, there were 4 cases of intraductal papilloma comprising around 12 % of benign breast lesions. All the four lesions were central papillomas and belonged to the age group of 25 to 46 years. Intraductal papilloma on histopathology is characterized by a fibrovascular core covered with both epithelial and myoepithelial cells. A variety of changes can accompany intraductal papilloma which includes sclerosis, epithelial or myoepithelial hyperplasia, atypical proliferation, and squamous or apocrine metaplasia.<sup>11</sup> In our study, histopathology of the lesions showed fibrovascular cores lined by myoepithelial cells with overlying epithelial cells. Areas of hemorrhage, necrosis and fibrosis were seen in one of the lesions. Apocrine metaplasia was seen in three lesions.

Lipoma is a common benign mesenchymal lesion of breast<sup>12</sup> Lipomas occur in patients of all ages, most cases being in adults aged 40-60.<sup>13</sup> Lipomas are composed of mature adipose tissue surrounded by a thin capsule; they are difficult to distinguish from normal breast tissue if a capsule is not detected.<sup>14</sup> In our study around 6 cases of Lipoma were seen in females in age range of 36 to 45. Histopathological examination showed sheets of adipocytes with eccentric nuclei. All the lesions showed partial or complete encapsulation.

Neurofibroma is common in the skin of the breast but is rarely found in the breast parenchyma, more common in females in the age range of 15-80 years.<sup>15,16</sup> In our study, 2 cases of Neurofibroma were seen in a 40 year old female and a 52 year old female. Histopathological examination revealed a spindle cell lesion with cells arranged in storiform pattern which were confirmed on IHC as neurofibroma.

Paget's disease represents 1-4 % of all Breast cancers. It affects men as well as women. The age range is 27-88 years.<sup>17,18</sup> The histological hallmark of the disease is the presence of Paget cells within the epidermis. These are large cells with abundant pale stained cytoplasm and large nuclei with prominent nucleoli, present singly in peripheral and superficial epidermis or in clusters in lower epidermis.<sup>19,20</sup> In our study, 2 cases of Paget's disease were seen in females aged 42 and 54 years old both in left breast. Histopathological examination showed large clear cells with hyperchromatic nuclei and prominent nucleoli in epidermis and was associated with in situ carcinoma of the same breast in one of the cases.

Smooth muscle tumors of the breast are rare (1%) and seem to affect only females in 4<sup>th</sup> -7<sup>th</sup> decades of life<sup>21</sup>. Leiomyoma is composed of spindle cells arranged in intersecting fascicles; cells have elongated cigar shaped nuclei with eosinophilic cytoplasm with absent or minimal nuclear atypia. Mitosis is sparse.<sup>22</sup> There were 2 cases of leiomyoma in a 35 year old female and a 40 year old female in our study of 4 years showing typical features of leiomyoma. One of the cases showed benign spindle cells without any atypia and mitosis and the other showed mild atypia but mitotic count was not increased.

Lymphoma rarely occurs as a primary tumor of the breast and represents only 0.1% -0.5% of all breast malignancies. B- cell lymphoma occur more frequently than T cell Lymphoma<sup>23</sup>. Primary breast lymphoma may manifest clinically as a palpable mass with or without skin changes that simulate inflammatory breast cancer. The age distribution of reported cases is wide (16-93 years)<sup>24,25</sup>. In our study, there was a single case of lymphoma over a period of 4 years found in a 50 year old female. It was a primary breast lymphoma. On microscopy, features were those of Diffuse Large B cell Lymphoma as was confirmed upon IHC.

Invasive Lobular carcinoma represents 5-15% of invasive breast tumors<sup>26,27</sup>. The mean age of patients with ILC is 57-65 years<sup>28</sup>. The classical pattern of ILC is characterized by a proliferation of small cells which lack cohesion and are individually dispersed or arranged in single file linear pattern in a fibrous connective tissue background.<sup>29,30</sup> In our study there were 4 cases of ILC that belonged to females >50 years of age. Sections showed cells with discohesive pattern of infiltration with oval nuclei, small amount of cytoplasm and intracytoplasmic lumina. One of cases showed features of solid

variant of ILC. Foci of Lobular carcinoma in situ were seen in one of the cases.

Metaplastic breast carcinoma account for 0.2-5% of all invasive breast cancers<sup>31</sup> In our study these comprised about 3% of the invasive breast cancers including non-miscellaneous ones which are not included in this study. Metaplastic carcinoma encompasses a group of neoplasms characterized by differentiation of neoplastic epithelium into squamous cells and/or mesenchymal looking elements<sup>32</sup>. Out of four cases there were 4 cases showing features of squamous cell carcinoma and 1 case showing predominantly spindle cell differentiation.

Primary breast fibrosarcoma is a rare neoplasm. Adem *et al.* reported that primary breast sarcoma comprised only 0.0006% of all breast malignancies presenting at his institution from 1940 to 1999.<sup>33</sup> The peak incidence of primary breast sarcoma occurs in the fifth and sixth decades of life<sup>34</sup>. Microscopic findings shows spindle cell tumor that has a cell pattern of columns of short parallel lines with all the lines in one column sloping one way and lines in adjacent columns sloping the other way.(herring bone pattern)<sup>35</sup> There was one case of fibrosarcoma belonging to a 56 year old female. Microscopically the tumor showed spindle shaped cells arranged in herringbone pattern with collagenous stroma. Few mitotic figures were seen along with few giant cells.

Medullary carcinoma is a rare and distinct subgroup of breast carcinomas accounting for less than 5% of all invasive breast cancers.<sup>36</sup> The patient's age at presentation is younger than that for invasive ductal carcinoma NOS, with a mean age ranging from 45 to 54 years<sup>37</sup>. As defined by the WHO<sup>38</sup> Medullary carcinoma should meet *all* of the following five morphologic criteria:1) Syncytial growth pattern in more than 75% of the tumor 2) No glandular or tubular structures, even as a minor component 3) Moderate to marked diffuse lymphoplasmacytic infiltrate in the stroma 4) Moderate to marked nuclear pleomorphism 4) Complete histologic circumscription. There were 3 cases of medullary carcinoma found in 40, 42 and 38 year old female in our study. In our cases, tumor showed circumscribed margin with syncytial growth pattern of the cells, vesicular nuclei, increased mitosis and inflammatory infiltrate.

Inflammatory carcinoma is a rare and aggressive type of breast cancer. It represents 1% to 6% of all cases of breast cancer.<sup>39</sup> The diagnosis is entirely based on clinical symptoms such as the rapid onset of signs like erythema and edema of the breast skin.<sup>40</sup> It has no specific diagnostic pathological criteria. Most Inflammatory carcinoma is a ductal carcinoma and has a high histological nuclear grade<sup>41,42</sup> There was a single case of inflammatory carcinoma with the clinical features of inflammatory carcinoma, microscopically showing high grade ductal carcinoma.

The WHO estimates that neuroendocrine carcinoma breast incidence varies between 0.3% and 0.5%. Histologically neuroendocrine tumors are characterized by uniform cells (round- or spindle-shaped), nuclear palisading, abundant finely granular eosinophilic cytoplasm, and nuclei with "salt and pepper" chromatin. Tumor cells form nests, islands, and alveolar-like structures surrounded by delicate fibrovascular stroma<sup>43,44,45</sup> There were two cases of neuroendocrine carcinoma breast in our study of 45 year old and 48 year old females. Sections showed uniform cells, growing in solid

nests, with eosinophilic cytoplasm and stippled chromatin. One of the cases showed high grade nuclear features.

## CONCLUSION

The female breast is affected by a wide spectrum of benign and malignant lesions many of which are rare. These lesions may be encountered upon the histopathological examination of breast biopsies and specimens by a pathologist. Many of these lesions benign as well as malignant may mimic each other on microscopic examination which makes it quite necessary for them to familiarize with them to arrive at a proper diagnosis and guide proper management.

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