

Original Research Article

Spindle cell lesions of breast: a retrospective analysis with emphasis on diagnostic challenges

Lekshmi Devi P.¹, Cicy P. J.^{1*}, Sansho E. U.², Deepa S.¹, Laila Raji N.¹

¹Department of Pathology, ²Department of General Surgery, Government Medical College Kottayam, Kerala, India

Received: 30 August 2017

Accepted: 28 September 2017

*Correspondence:

Dr. Cicy P. J.,

E-mail: elavumkal@gmail.com

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ABSTRACT

Background: Spindle cell lesions of breast comprise a rare group of complex entities which may be reactive, benign or malignant. Though definitive diagnosis is difficult especially in small biopsies, it is of utmost importance since the management differs. Precise knowledge of the lesions in this group, thorough sampling, clinic radiological correlation and ancillary techniques will aid in making the correct diagnosis. Review of literature showed only a few extensive studies on spindle cell lesions in breast, especially from South India.

Methods: Our research is a descriptive histopathological analysis of 55 cases of spindle cell lesions of breast, done over a 2-year period from Jan 2015 to Dec 2016 in the Pathology department, of our institution.

Results: A total of 55 cases were received. The reactive spindle cell proliferations were Diabetic mastopathy, Pseudoangiomatous stromal hyperplasia, and sclerosing adenosis. Benign phyllodes tumour, spindle cell lipoma and neurofibroma comprised the benign category. The malignant lesions included metaplastic carcinoma, malignant phyllodes tumour and sarcoma.

Conclusions: Benign lesions constituted the majority (60%) in our study. Of these, benign phyllodes tumour constituted the majority, 41.8% of the total cases. The remaining 40% were malignant spindle cell neoplasms, of which metaplastic carcinoma was the single largest group accounting for 29.1%. Since reactive and benign spindle cell lesions may show atypia, definitive diagnosis should be made only after considering atypical mitotic figures, presence of necrosis and imaging findings. A wide excision with adequate margins is necessary in incision biopsies with suspicious findings.

Keywords: Breast, Metaplastic carcinoma, Phyllodes tumour, Spindle cell lesions

INTRODUCTION

Spindle cell lesions of breast are rare compared to epithelial lesions of breast. They can be reactive, benign or malignant lesions constituting a diverse group with overlapping clinical, radiological, histopathological and immunohistochemical findings, making the diagnosis challenging. A proper knowledge of the different lesions which come under this group is of utmost importance since the behaviour and treatment modalities are different. An algorithmic approach considering cell

morphology, presence and degree of atypia, growth pattern, mitotic activity and clinicoradiological correlation for apt diagnosis has been proposed.¹ A detailed gross examination is necessary especially in biphasic tumours like phyllodes tumour which may be misdiagnosed in core biopsies.²

All breast lesions with a mesenchymal component will come under the category of spindle cell lesions of breast. According to the WHO classification, the main benign spindle lesions in our study will come under the

mesenchymal lesions of breast.³ Though phyllodes tumour comes under fibroepithelial lesions, it is included in our study since it has a predominant stromal component.³

METHODS

The present study is a descriptive analysis of 55 cases of spindle cell lesions of breast received over a period of 2 years from Jan 2015 to Dec 2016 in the department of pathology government medical college, Kottayam, a tertiary care centre in south India. Trucut biopsies, lumpectomies and mastectomy specimens were included in our study. All cases showing predominant spindle cell morphology were included in the study. Fibrosis which occurred as a part of inflammation or post treatment was not included in our study. The Haematoxylin and Eosin stained slides were analysed and serial sections were taken in relevant cases. The relevant clinical details and imaging findings were retrieved from the data entered in the registers. Data analysis was done using SPSS 16 software and the frequency tables were calculated.

RESULTS

Out of 789 breast lesions, total of 55 cases of spindle cell lesions (7%) were received in our department during this study period. Among the 55 cases, 33 cases (60%) were in the benign category and 22 cases in the malignant category (40%). The age range was from 29-70years, with peak incidence at 50years. There was greater predilection of involvement in the left breast (61. 8%). The size of lesions varied from 1.5-30cms. Benign phyllodes tumour accounted for the majority of lesions (41.8%), followed by metaplastic carcinoma of breast (29.1%).

Table 1: Spindle cell lesions of breast.

Diagnosis	Number of cases	%
Benign phyllodes	23	41.8
Diabetic mastopathy	4	7.3
Pseudoangiomatous stromal hyperplasia	2	3.6
Sclerosing adenosis	2	3.6
spindle cell lipoma	1	1.8
Neurofibroma	1	1.8
Metaplastic carcinoma	16	29.1
Malignant phyllodes	4	7.3
Malignant spindle cell neoplasm	2	3.6
Total	55	100.0

The reactive lesions observed in our study were Pseudoangiomatous stromal hyperplasia (PASH) (2 cases), diabetic mastopathy (DM) (4 cases) and sclerosing adenosis (SA) (2 cases).

Benign phyllodes tumour, neurofibroma and spindle cell lipoma comprised the benign category. The malignant ones were metaplastic carcinoma (16 cases), malignant phyllodes tumour and sarcomas (Table 1).

Benign spindle cell lesions

Benign phyllodes tumour

These accounted for majority of benign lesions. The age group varied from 34 to 70 years, with peak incidence at 46 years. There was greater predilection on the left breast, 56.5 % (n=13 cases). Of the 23 cases, 3 cases were trucut biopsies hence the tumour size and resection margins could not be assessed in these 3 cases. The gross specimens of all were well circumscribed masses. The tumour size ranged from 1.5cms to 26cms. Margins of resection were free in 10 cases, 5 cases showed close margins (<1mm) and in 5 cases margins were involved. Majority of the cases had solid gross appearance with four showing cystic degeneration. Two cases showed areas of infarction. Microscopy showed the characteristic leaf like fronds lined by epithelium with subepithelial accentuation of stromal cellularity (Figure 1a). Epithelial changes like adenosis, apocrine change, epitheliosis and papillomatosis were seen in 4 cases and stromal changes like atypia and lipomatous metaplasia in 2 cases.

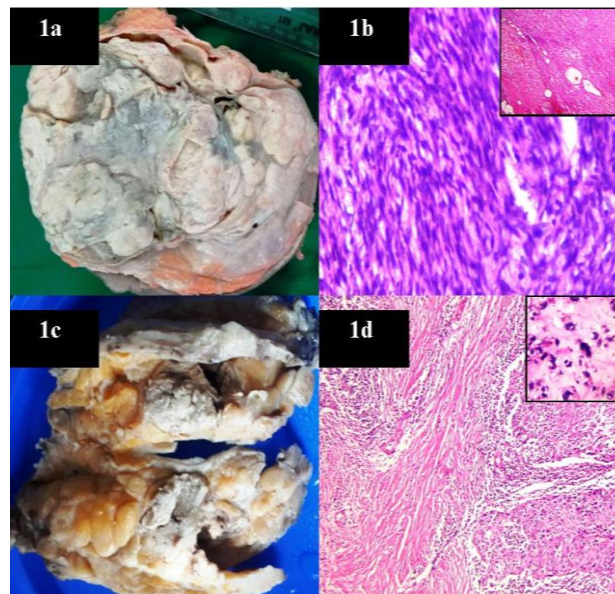


Figure 1: Is a photomicrograph of benign cases. 1a: Benign phyllodes tumour showing characteristic subepithelial accentuation and stromal cellularity. H and E 100X. 1b: Diabetic Mastopathy showing the characteristic stromal fibrosis and epitheloid myofibroblasts H and E 100X. Inset showing lymphocytic infiltrate H and E 400X. 1c: Spindle cell lipoma showing bland spindle cells and adipocytes H and E 100X. Inset showing ropy collagen H and E 400X. 1d: PASH- dense collagenous stroma with formation of slit like spaces lined by spindly cells. H and E 100X. Inset H and E 400X

Diabetic mastopathy

All the 4 cases were chronic diabetic patients who presented with complaints of breast lump. One patient had hypertension and hyperlipidaemia also. Of the 4 cases, two cases had bilateral involvement. The size varied from 2cms to 8cms and appearance was homogenous whitish. Microscopy showed extensive fibrosis and periductal, perivascular and lobular lymphocytic infiltrate (Figure 1b).

Other lesions

2 cases of PASH presented as masses of 8 and 10cm with clinical suspicion of neoplasm but histopathology showed dense collagenous stroma with characteristic slit like spaces (Figure 1d). Two cases of sclerosing adenosis showed grey white areas of 2-1.5cm in histopathology. The remaining two cases included a case of spindle cell lipoma showing, adipocytes, spindle cell areas and the characteristic ropy collagen (Figure 1c) and a case of neurofibroma.

Malignant spindle cell lesions

In the category of malignant spindle cell lesions, metaplastic carcinoma constituted the largest category (73%), followed by malignant phyllodes (18%) and other malignant spindle cell neoplasms (9%).

Metaplastic carcinoma (MCB)

Of the 16 cases, 4 were trucut biopsies and the remaining 12 were mastectomy specimens. The age range varied between 34 and 67years. The right to left ratio was 12:4. The tumour size ranged from 1-10cms. All cases were seen as grey white firm to hard masses with infiltrative borders, with cystic degeneration in 5 cases (Figure 2c). In the cases diagnosed on trucut biopsy there was malignant mesenchymal and epithelial components, but presence of other heterologous areas was not seen. However, of the 12 metaplastic carcinomas (mastectomy specimens), malignant spindle cell areas comprised the main mesenchymal component (10 cases), five cases showed squamous areas and one each showed chondroid differentiation and osseous differentiation (Figure 2d). Four cases showed lymph node metastases. Lymphovascular invasion was present in 6 cases. Immunohistochemistry (IHC) studies showed 7 triple negative cases, 3 ER only positive and 2 ERPR positive cases. IHC was not available in 4 cases.

Malignant phyllodes tumour

There were four cases and age range were from 40 to 50years. Tumour size varied from 8.5-30cms and gross showed fleshy appearance with pushing margins and cleft like spaces. (Figure 2a). Two cases were recurrences, one after 3years and other after 2years. Both had incomplete resected margins on prior surgery. The tumour with 30cm

size showed infiltration into muscles of chest wall. Microscopy showed malignant spindle cell stroma (Figure 2b). There was no lymph node involvement.

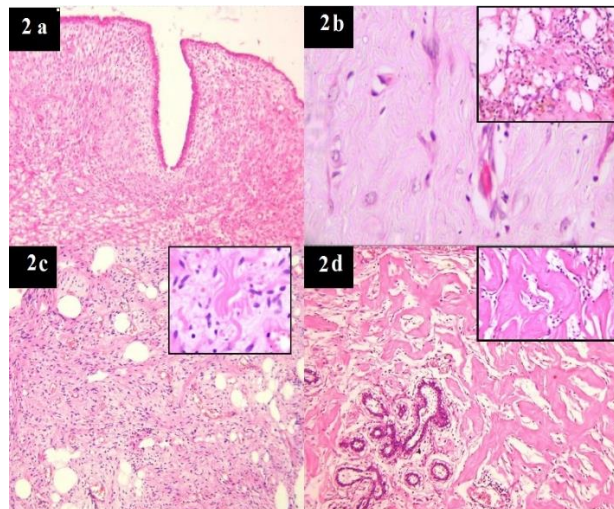


Figure 2: is a photomicrograph of malignant lesions. 2a: Gross of malignant phyllodes tumour with fleshy cut surface showing clefts. 2b: Histopathology of malignant phyllodes tumour showing atypical stromal cells H and E 400X. Inset showing infiltration to skeletal muscle. H and E 100X. 2c: Gross picture of metaplastic carcinoma breast showing infiltrative margins with solid and cystic cut surface. 2d: Histopathology showing malignant squamous component in metaplastic carcinoma breast H and E 100X. Inset showing chondroid differentiation H and E 400X.

Other lesions

The remaining 2 cases were diagnosed as malignant spindle cell neoplasm with high grade nuclear features. No epithelial elements were identified even after extensive sampling. IHC studies were positive for vimentin, desmin and SMA, negative for ER, PR, HER 2, S100, p63 and CK in one case favouring diagnosis of sarcoma with smooth muscle origin. The other showed positivity for vimentin, CD34 and SMA only but negative for desmin, ER, PR, HER 2 and CK favouring a myofibroblastic origin. Comparison of the gross appearance and histopathology features of the different spindle cell lesions in our study are summarized in Table 2.

DISCUSSION

The diagnosis of spindle cell lesions of breast is challenging since some of these diverse entities have similar clinical and radiological features. The main cause of diagnostic complexity in the approach to spindle cell lesions of breast is the necessity of providing a proper correlation between clinical, radiological, morphological and immunohistochemical findings.² Histopathology is

the gold standard for diagnosis and immunohistochemical confirmation will be necessary in certain cases like

malignant phyllodes, metaplastic carcinoma and spindle cell lipoma.

Table 2: Comparison of the gross appearance and histopathology features of the different spindle cell lesions of breast.

Diagnosis	Gross	Histopathology	Margins	Lymph node involvement
Benign phyllodes	Solid grey white fleshy with clefts cystic +/-	Stromal cellularity with subepithelial accentuation epithelial changes +/-	Circumscribed but pushing margins	Absent
Diabetic mastopathy	Solid grey white homogenous	Fibrosis, periductal, perivascular and lymphocytic infiltrate and lobular atrophy	Fairly circumscribed	Absent
Pseudoangiomatous stromal hyperplasia	Grey white	Dense sclerosing stroma with slit like spaces lined by bland spindle cells	Fairly circumscribed	Absent
Sclerosing adenosis	Grey white	Compressed and distorted acini with surrounding dense stroma.	Fairly circumscribed	Absent
spindle cell lipoma	Grey white	Benign spindle cells, adipocytes, ropy collagen	Fairly circumscribed	Absent
Neurofibroma	Grey white	Benign spindle cells	Fairly circumscribed	Absent
Metaplastic carcinoma	Solid grey white Cystic +/-	Malignant spindle and epithelial component squamous differentiation +/- heterologous elements +/-	Infiltrative margins	+/- Present in 4cases
Malignant phyllodes	Grey white Cystic +/-	Malignant spindle and benign epithelial component squamous differentiation absent heterologous elements +/-	Pushing margins	Absent
Malignant spindle cell neoplasm	Grey white Cystic +/-	Malignant spindle cells .no epithelial component	Infiltrative margins	+/-

Of the total 55 cases of spindle cell lesions of breast included in our study conducted over a period of 2 years, there were 33 cases in the benign category (60%) and 22 (40%) cases in the malignant category. Phyllodes tumour constituted the main lesion in the benign category. There were 23 cases of benign phyllodes tumour (70%), the other entities were diabetic mastopathy (12%), Pseudoangiomatous stromal hyperplasia (6%), sclerosing adenosis (6%) spindle cell lipoma (3%) and neurofibroma (3%) (Figure 3).

The architectural hallmark of leaf- like fronds surmounted by benign glandular epithelium serves to delineate phyllodes tumour from its mimics. But some cases of malignant phyllodes tumour may show prominent stromal overgrowth to the extent that epithelial components are found only after detailed sampling, extensive search and study of many serial sections.⁴ Of the 23 cases of benign phyllodes tumour we studied, two showed areas of infarction.

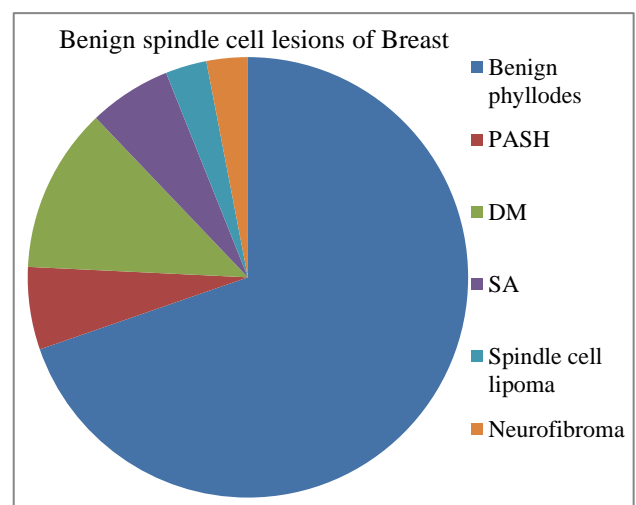


Figure 3: Relative frequency of benign spindle cell lesions.

However, histopathology did not show any atypical stromal cells or increased mitotic figures. One case of infarction was FNA induced. The microscopic features of all cases showed the characteristic stromal preponderance, leaf like fronds and benign epithelial components. However, one case showed stromal atypia, and another showed lipomatous stromal metaplasia on microscopy.

As per certain studies, PASH is an infrequent but not rare major pathologic finding present in around 6% of benign surgical breast biopsies.⁵ This benign mesenchymal lesion of breast has dense collagenous stroma and capillary-like spaces lined by slender stromal cells as the characteristic histopathological feature and was first described by Vuitch et al.⁶ It affects women of reproductive age group and has a possible hormonal aetiology. It may be an incidental finding but rarely presents as a palpable mass when it is called tumorous or nodular PASH.

In our study both cases presented as palpable masses clinically mimicking neoplasm. One patient was premenopausal, but the other was postmenopausal. Due to presence of slit like spaces lined by spindly cells, angiosarcoma forms an important differential diagnosis on histopathology.⁷

Diabetic mastopathy is a rare fibroinflammatory disease of breast seen in diabetic women of pre-menopausal age.^{8,9} It is thought to result from the resistance to collagen degradation in persons with diabetes. This uncommon fibrous proliferation may mimic a neoplasm as it clinically presents as single or multiple nontender firm to hard mass. Mammography may not be helpful since the glandular tissue may mask the lesion.⁸ However on MRI, it is seen as an enhancing lesion and specific parenchymal enhancement may help to differentiate it from carcinoma.^{10,11} Grossly they are seen as firm homogenous masses with histopathology showing marked fibrosis and lymphocytic infiltration. Lobular atrophy and presence of epithelioid myofibroblasts are other characteristic features.^{9,12}

Tse et al has proposed a simplified approach if faced with an atypical spindle cell proliferation, to evaluate two principle components of the lesions, namely spindly cells and epithelial cells. The spindle cell proliferation can have a bland morphology or can be pleomorphic, and they may be mixed with an epithelial component, which may be benign or malignant.¹³ Based on this criterion, the spindle cell lesions may be categorized into four groups

- Biphasic lesions having predominant spindle cell component with benign epithelial (ductal) component e.g., fibroadenomas, Phyllodes tumours, PASH, adenomyoepithelioma,
- Biphasic lesions having predominant spindle cell component with malignant epithelial (ductal)

component e.g., biphasic metaplastic carcinoma with a ductal component,

- Monophasic lesions with pure pleomorphic spindle cells only e.g., monophasic metaplastic carcinoma, sarcomas like angiosarcoma, malignant fibrous histiocytoma,
- Monophasic lesions with pure bland spindle cells only e.g., fibromatosis like metaplastic carcinoma, fibromatosis and other unusual conditions like dermatofibrosarcoma protruberance.

Rungta et al has stressed the importance to distinguish between metaplastic carcinoma and malignant Phyllodes tumours of the breast as there is significant difference in the management and prognosis. The characteristic leaf-like architecture and lack of cytokeratin expression favours a diagnosis of phyllodes.¹⁴

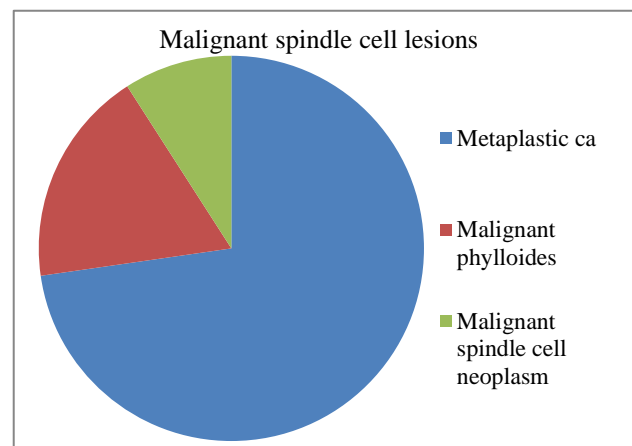


Figure 4: Relative frequency of malignant spindle cell lesions.

Metaplastic carcinomas with high grade nuclear features and heterologous differentiation can be readily diagnosed as malignant, but the spindle cell variant of MCB can cause diagnostic dilemma and may even be mistaken for fibrosis due to scarring, nodular fasciitis, fibromatosis or fibrosarcoma.^{15,16}

In our series one case of metaplastic carcinoma showed only malignant stromal component in core biopsy and epithelial elements were found only after extensive sampling of mastectomy specimen. So, in core biopsy it was signed off as malignant spindle cell neoplasm with metaplastic carcinoma and malignant phyllodes as differentials.

The possibility of a malignant phyllodes tumour is more than a pure sarcoma when prominent stromal component is seen and a diligent search for benign epithelial component should be attempted. Along with this, a judicious use of IHC will help to clinch the correct diagnosis.

CONCLUSION

Diagnosis of spindle cell lesions of breast can be challenging since some of the benign lesions may mimic carcinoma clinically and on imaging. Hence detailed sampling from different areas should be done on wide excision or mastectomy specimens and ancillary studies like immunohistochemistry should be done in relevant cases.

ACKNOWLEDGEMENTS

Authors would like to acknowledge Smt. Kalakumary and Smt. Susan for their assistance.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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Cite this article as: Devi LP, Cicy PJ, Sansho EU, Deepa S, Laila RN. Spindle cell lesions of breast-a retrospective analysis with emphasis on diagnostic challenges. *Int J Adv Med* 2017;4:1627-32.