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Original Research Article

A clinical, cyto-histopathological and immunohistochemical study of spindle cell lesions of breast in a tertiary care hospital

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ABSTRACT

Aim and Objective: Spindle cell lesions in the breast are a diverse group of entities that can be either benign or malignant. Spindle cell lesions often pose a challenge to the diagnosing clinician because of the vast differential diagnoses, the rarity of these lesions and the histological similarities. We aim to conduct this study to profile these rare lesions of the breast and correlate the cyto-histopathological features on FNAC with immunohistochemical characteristics to determine its efficacy.

Materials and Methods: A total 260 patients, suffering from spindle cell lesions of the breast, attending the outpatient and in-patient services were included in this 5 year study (3 years of retrospective cases and 2 years of prospective cases) conducted at Department of Pathology, JNMCH, AMU, Aligarh.

Inclusion criteria: Only Diagnosed cases of Spindle cell lesions of breast were included in the study. The study sample comprised of 260 cases (105 cytological cases and 220 histopathological cases with 65 cases that are common to both)

Exclusion criteria: Apart from diagnosed cases of Spindle cell lesions of breast all other breast lesions either reactive benign or malignant were excluded.

Results: Total number cases of breast lesions received in the Department of Pathology during 5 year study period were 15,270 out of which 9700 cases were of Histopathology and 5570 were of Cytopathology. Among 15,270 cases, a total number of 15,010 (98.29%) cases belonged to non-spindle cell lesions which were excluded from the study and the remaining cases i.e., 260 (1.7%) cases diagnosed as spindle cell lesions of breast constituted the study group. Of the total260 cases, 105 cases were of cytopathology and 220 cases were of histopathology and cases common to both i.e., those cases which had cyto-histopathological correlation were 65 cases (20%). The highest incidence of spindle cell lesions occurred in 4^{th} decade of life comprising of 126/260 cases (48.46%).

Conclusion: Spindle cell lesions are not so common in breast, accounts for 1.7% of cases only. The workup involves thorough histopathological examination due to considerable morphological overlap and an elaborate IHC studies since no single Immunohistochemical marker is sufficient/specific to clinch the final diagnosis. Hence, it is difficult to make the final diagnosis of spindle cell lesions of breast on histopathology alone in majority.

1. Introduction

Breast Cancer is the most common cancer diagnosed in women, accounting for 1 in 10 cases of cancer diagnosed every year. Breast tissue is prone to develop benign

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and malignant changes. GLOBOCAN 2020 reports breast cancer as the most common cancer worldwide and fifth most common, death causing cancer globally.[1]

Recent studies from India suggest that Breast Cancer is the leading cause of cancer death in women surpassing the previous widely recognised Cervical Cancer as the leading cause with age adjusted rate as high as 25.8 per 100,000 women and mortality 12.7 per 100,000 women.[2]

Spindle cell lesions of the breast include a diverse group of entities sharing common histopathological features. These rare lesions mimic clinically and radiographically the common benign lesions of the breast (eg, fibroadenomas) or may appear falsely malignant. Spindle cell lesions often pose a challenge to the diagnosing clinician because of the vast differential diagnoses, the rarity of these lesions and the histological similarities.

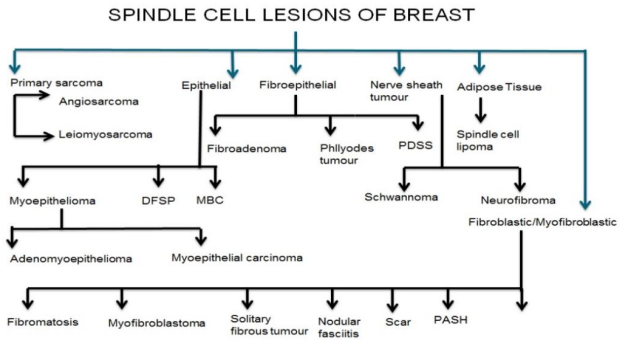

Figure 1: According to (Charu et al., 2017)[3] spindle cell lesions can be categorised as under.

Fine Needle Aspiration Cytology (FNAC) can be helpful in the diagnosis of these breast lesions by combining its results with clinical and radiological features. An important adjunct could be to determine if these lesions have only spindle cells or if other components such as epithelial cells are present. Whether the lesions appear bland or pleomorphic on FNAC, the diagnostic accuracy of these lesions and thus the patient outcomes can be improved.[4,5]

Immunohistochemistry is a good diagnostic tool for the diagnosis of bland appearing spindle cell lesions. As no immunohistochemistry marker is completely sensitive and specific, it would be appropriate to conclude that using a panel of antibodies would yield the best results. Interpretation of the results of immunohistochemistry should take into account the cytological features of the lesion as well. A suspected spindle cell carcinoma should be tested using a panel of antibodies against epithelial markers: both low and high molecular weight cytokeratin.[4,6]

The diagnostic challenges that these lesions pose due to diversity of the features on cytomorphology with focal nature of the diagnostic and prognostic histochemical properties, we aimed to conduct this study to profile these rare lesions of the breast and correlate the cyto-histopathological features on FNAC with immunohistochemical characteristics to determine its efficacy.

2. Materials and Methods

The present study entitled, "A Clinical, Cyto-Histopathological and Immunohistochemical study of Spindle Cell Lesions of Breast" included 260 patients, suffering from spindle cell lesions of the breast, attending the outpatient and in-patient services of the Department of Surgery at Jawaharlal Nehru Medical College & Hospital (JNMCH), Aligarh Muslim University, Aligarh. The cytological and histopathological examinations were carried out in the Department of Pathology, (JNMCH). Relevant clinical history and examination findings were also recorded. Three years of retrospective cases and two years of prospective cases i.e. total 5 years cases were included in this study.

2.1. Inclusion criteria

Only Diagnosed cases of Spindle cell lesions of breast were included in the study. The study sample comprised of 260 cases (105 cytological cases and 220 histopathological cases with 65 cases that are common to both).

2.2. Exclusion criteria

Apart from diagnosed cases of Spindle cell lesions of breast all other breast lesions either reactive benign or malignant were excluded.

A detailed patient's clinical history, examination, relevant investigations and gross specimen findings were recorded in each case. Clinical examination was focussed mainly on local examination of the breast and regional lymph node status.

Fine needle aspiration cytology (FNAC) was performed on patients with palpable lumps in breast and image guided FNAC was done for deep seated breast lesions. For retrospective analysis cytological smears and related paraffin blocks and slides were obtained from the record section of cytology and histopathology division of the Department of Pathology.

FNAC from the palpable breast lump was done with 22 gauge needle and smears prepared were stained with H&E and Pap stains. For retrospective study, already diagnosed cases of spindle cell lesions of breast were obtained from archive of cytology lab and all slides reviewed.

Lumpectomy/Mastectomy and tru-cut biopsy specimens with or without axillary lymphadenectomy were fixed in 10% neutral buffered formalin (10ml of 40% formaldehyde diluted in 90ml of water). Sections from the relevant areas were taken and submitted for further processing as per routine departmental laboratory protocol. After fixation, tissue pieces were processed in Automated Tissue Processor

set, LEICAM TP1020 (Germany), for a 24-hour cycle. The sections were mounted onto clean glass slides coated with albumin and stained with routine H&E stain using Harris Haematoxylin and aqueous Eosin.

The slides thus obtained, were examined under the light microscope to study the morphological details of the lesions and were carefully recorded. Sections most suited for immuno-histochemistry (IHC) were selected and the corresponding blocks were submitted for section preparation.

Microscopic evaluation was done using Olympus CH21i microscope with a high power field (40X) diameter of 0.44 mm and the corresponding field area of 0.152 mm. FNA smears stained by H&E and Pap stains were examined to assign diagnosis. H&E stained histological sections were assigned diagnosis according to WHO classification of tumors of the breast (2019).[7]

2.3. Statistical analysis

The statistical analysis was carried out using Statistical Package for the Social Sciences (SPSS) software (v.20. USA) to determine Sensitivity, Specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV), and Accuracy. Descriptive numerical data was tabulated as numbers and percentages. Pictorial representations in the form of bar diagrams and pie charts were provided wherever necessary.

3. Results

Total number cases of breast lesions received in the Department of Pathology during 5 year study period were 15,270 out of which 9700 cases were of Histopathology and 5570 were of Cytopathology. Among 15,270 cases, a total number of 15,010 (98.29%) cases belonged to "non spindle cell lesions" which were excluded from the study and the remaining cases i.e., 260 (1.7%) cases diagnosed as spindle cell lesions of breast constituted the study group. Of the total 260 cases, 105 cases were of cytopathology and 220 cases were of histopathology and cases common to both i.e., those cases which had cyto-histopathological correlation were 65 cases (20%). Of the 260 cases of breast spindle cell lesions, all patients were female and no case was found in the male sex. Out of 260 cases the most common clinical complaint was breast lump in 240 cases (92.3%) followed by pain and mastalgia in 104 cases (40%) (Table 1).

Out of 105 cases received in cytopathology, 70 (66.7%) cases were diagnosed as benign spindle cell lesions, whereas 25 (23.8%) cases were malignant and 10 (9.52%) cases were inconclusive for any opinion (Table 2).

Whereas Out of 220 cases received in histopathology, 148 cases (67.3%) fell broadly into benign category whereas 42 (19.1%) cases were diagnosed as malignant spindle cell lesions, followed by 30 (13.6%) cases wherein the diagnosis rendered was either a borderline spindle cell malignancy or a low grade malignancy (Table 2).

In our study, highest incidence of Spindle cell lesions of breast on cytopathology was observed in age group of 40-49 years with total 52 cases (49.52%) (35 cases were benign, 15 cases were malignant and 02 cases were inconclusive) followed by age group of 30-39 years with total 30 (28.5%) cases (22 cases were benign, 02 were malignant and 06 were inconclusive). No spindle cell malignancy cases was found in the age group of <20 years (Table 3).

Of 105 cases, a diagnosis of spindle cell lesion of breast was rendered in 65 cases (62%) on cytology favouring a "benign spindle cell lesion" in 40 cases (38%) and a "malignant spindle cell lesion" in 25 cases (24%). In rest 30 cases (28.5%) cytological diagnosis was a "benign phyllodes tumor". In 10 cases cytological findings were inconclusive for any opinion (Table 4).

In our study, highest incidence of Spindle cell lesions of breast diagnosed on Histopathology was observed in age group of 40-49 years with total 74 cases (33.6%) (55 cases were benign, 11 cases were malignant and 8 cases were of borderline category) followed by age 30-39 years with total 51 cases (23.1%) (40 cases were benign, 05 malignant and 06 borderline lesions). Least number of cases i.e., 13 cases falling in benign category were found in <20 years of age with no observed malignant and borderline malignant lesions in this age group (Table 5).

Out of 220 histopathologically diagnosed cases, benign phyllodes tumor was the most common entity comprising of 85 cases (38.6%). Other tumors in benign category were 15 cases (6.8%) of PASH, 13 cases (6%) of Myofibroblastoma, 12 cases (5.4%) of Nodular Fasciitis and 10 cases (4.54%) of desmoid type fibromatosis and 4 cases (1.81%) of Inflammatory myofibroblastic tumor. Borderline phyllodes tumor was the most common entity in intermediate category with total 30 cases (13.7%). In malignant category malignant phyllodes tumor was the most common tumor accounting for 25 cases (11.4%) followed by metaplastic carcinoma with total 13 cases (6%) and myxofibrosarcoma 3 cases (1.36%). Less common entities encountered were DFSP, neurofibroma, schwannoma and spindle cell lipoma (Table 6).

3.1. Cyto-histopathological correlation

Of the total 220 cases in 65 cases a correlation of cytological diagnosis with histopathological diagnosis was attempted. In 60 cases (92.3%) diagnosis made on cytology correlated well with the diagnosis rendered on histopathology (Table 7).

However cases of benign phyllodes were inconclusive on FNA while in two cases FNA smears were blood contaminated, so in these 5 cases correlation was not possible. The diagnosis made on cytology correlated well with the diagnosis made on histopathology in 60 cases

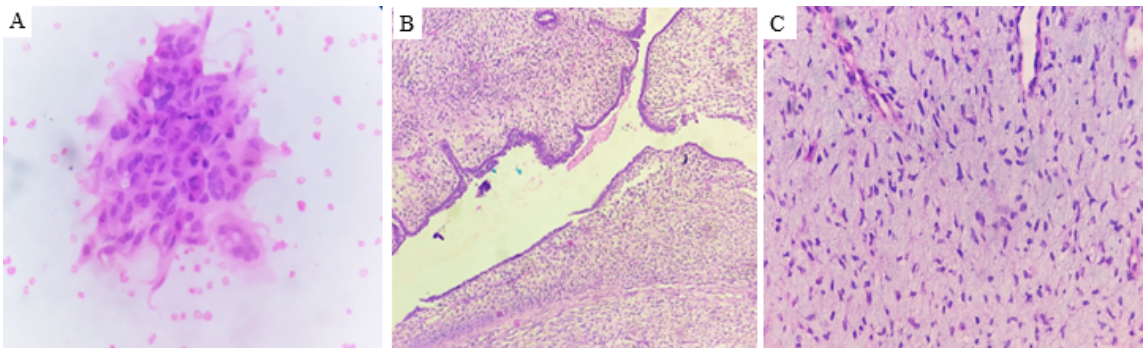

Figure 2: A: FNA smear showing cellular stromal fragments and sheets of benign spindle cells favouring a cytological diagnosis of benign spindle cell tumor/ Benign phyllodes tumor. (H&E 20x); **B,C:** H&E sections of Benign Phyllodes Tumor showing proliferation of stromal spindle cells and myxoid changes in stroma. Mitosis and necrosis were absent. (10x and 20x)

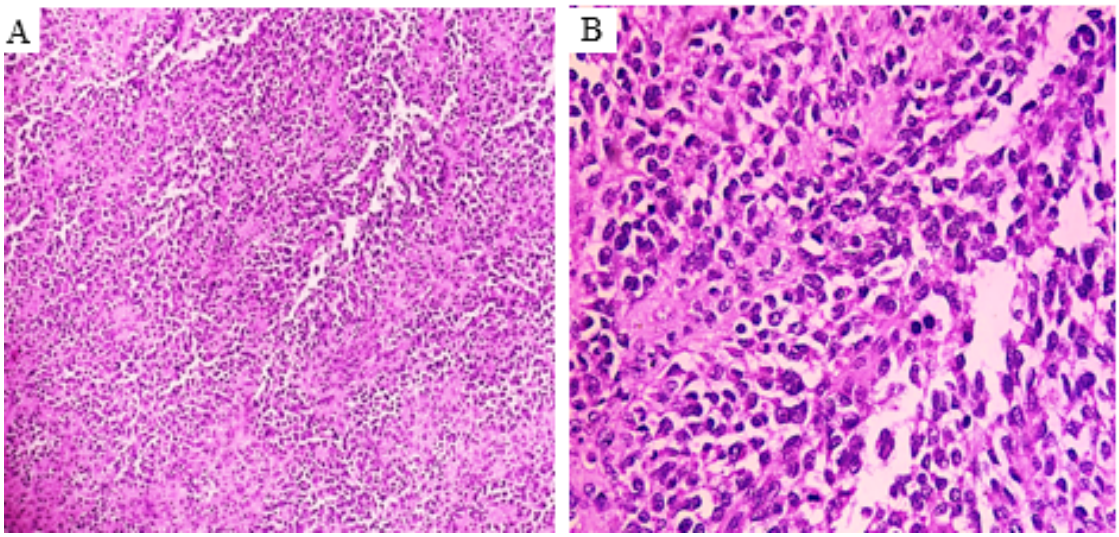

Figure 3: A,B: Corresponding H&E section of Malignant Phyllodes Tumor showing sheets & papillae of atypical spindle cells with oval / round vesicular to hyperchromatic nuclei, prominent nucleoli and moderate eosinophilic cytoplasm. Mitosis was also present frequently. (H&E 10x and 40x)

Table 1: Distribution of spindle cell lesions of breast according to presenting clinical complaints (n= 260)

Complaints	No. of cases (n=260)	Percentage
Breast mass/lump	240	92.3%
Pain/mastalgia	104	40%
Ulceration/ fungating mass breast	54	20.7%
Nipple retraction	20	7.6%
Nipple discharge	42	16.1%
With Axillary Lymphadenopathy	80	30.7%

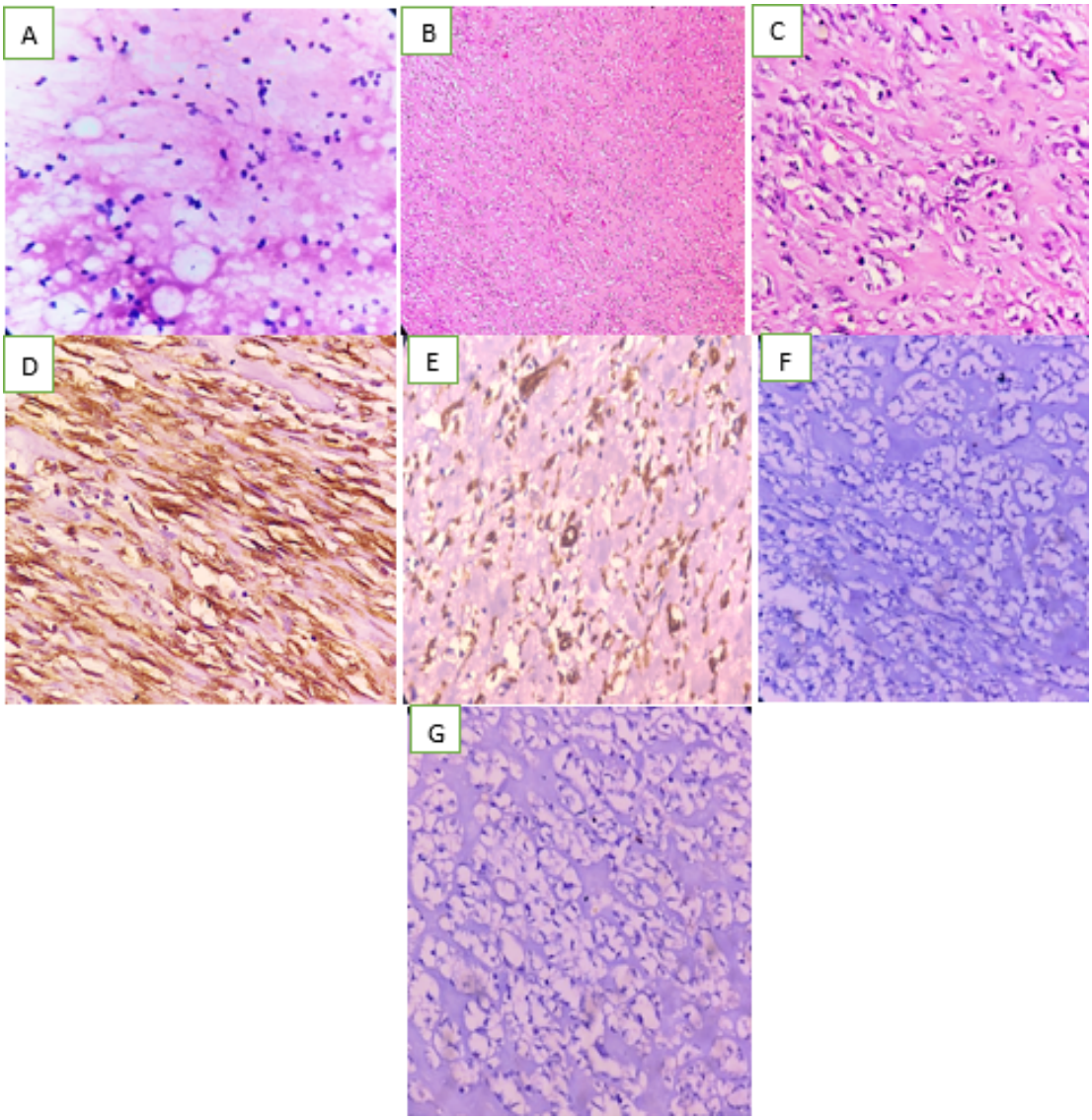

Figure 4: A,B: FNA smear of Benign spindle cell lesion of breast showing bland oval to spindlecells lying singly and in loose clusters of fat mixed myxoid background. (H&E 20x); **B,C:** Corresponding H&E section of Myofibroblastoma showing tumor cells composed of spindle to oval cells arranged in short haphazardly intersecting fascicles of spindle shaped cells separated by band of eosinophilic collagen. (H&E 10x and 40x); **D,E:** Cytoplasmic positivity of both SMA and Vimentin in tumor cells of Myofibroblastoma (IHC 40x); **F,G:** Myofibroblastoma Pan Ck and CD34 negative in tumor cells. (IHC X 20X)

with few discordant cases. Forty nine cases (81.7%) were benign and nine cases (15%) were malignant both on cytology and histopathology. However in 2 cases, the diagnosis made on cytology did not correlate with histopathology since in 1 case the cytological diagnosis rendered was a benign spindle cell neoplasm which turned out to be a malignant phyllodes tumor on histopathology and in another case, initially a cytological diagnosis of malignant spindle cell neoplasms was made which on subsequent histopathological examination turned out to be benign phyllodes tumor. Therefore a positive correlation (concordance) was found in 58 cases (96.6%) whereas 2 cases (3.4%) were discordant (Table 7).

Therefore, Sensitivity, Specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV) and Diagnostic Accuracy of FNAC in diagnosing spindle cell tumors of breast came out to be 98%, 90%, 98%, 90% and 96.67% respectively (Table 8).

3.2. Histopathology and immunohistochemistry corroboration

Of the total 220 cases of spindle cell lesions of breast received in histopathology, Immunohistochemical (IHC)

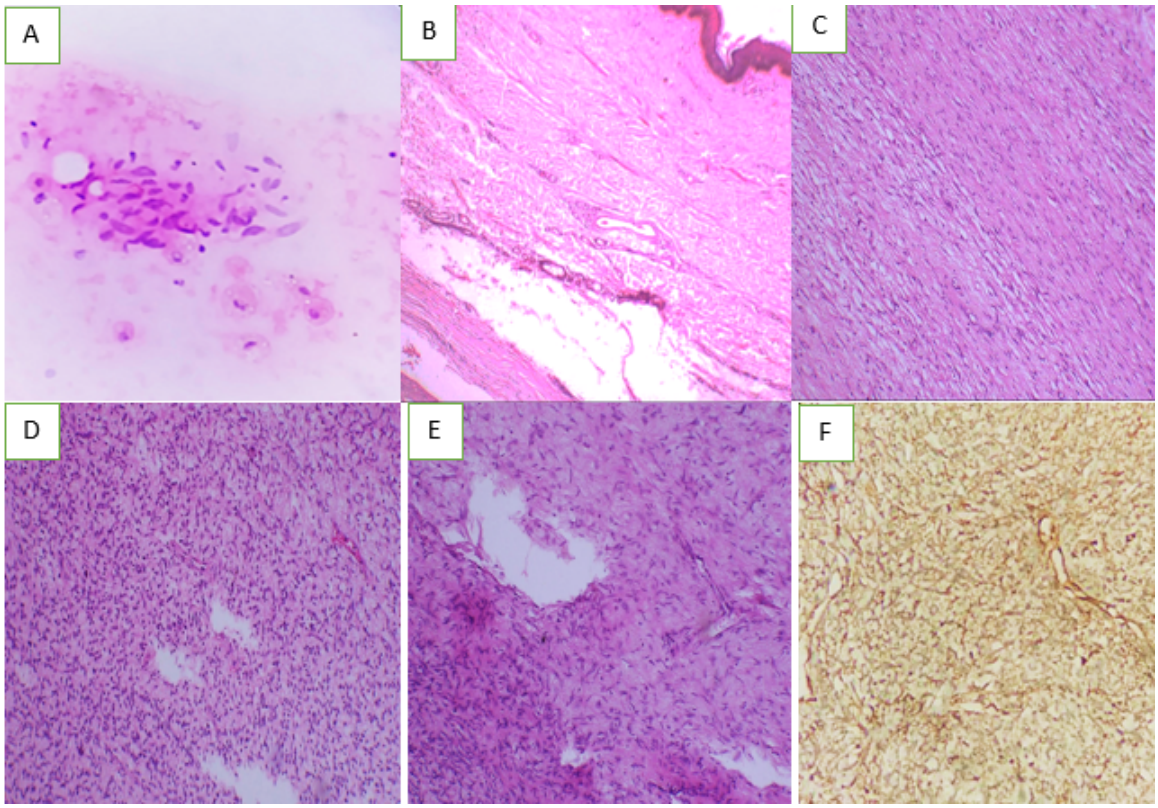

Figure 5: A: FNA smear of Nodular Fasciitis showing cluster of bland appearing spindle cells along with mild lymphocytic infiltrate in background. (H&E 20x); **B,C:** Corresponding H&E section of Nodular Fasciitis showing bland spindle to oval cells arranged in short fascicles to storiform pattern (feathery growth). (H&E 10x and 20x); **D,E:** Corresponding H&E section of Nodular Fasciitis showing bland oval to stellate cells arranged in short fascicles to storiform pattern (feathery growth) along with areas of haemorrhage and lymphocytic infiltrate in background. Mitosis and necrosis were absent. (H&E 10x and 20x); **F:** Nodular Fasciitis SMA positive (cytoplasmic staining). (IHC X 20x)

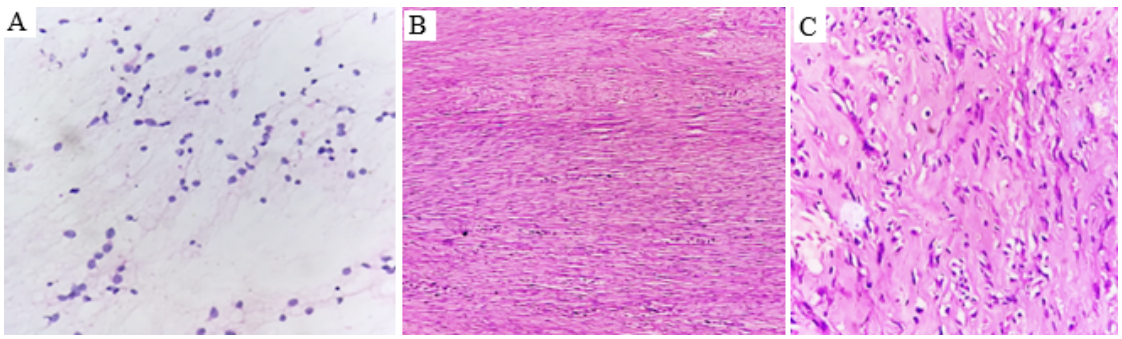

Figure 6: A: FNA smear of Desmoid Type Fibromatosis Breast showing isolated plump fibroblasts without atypia, along with heterogeneous population of lymphocytes, and a few stromal fragments in a proteinaceous background. (H&E 20x); **B,C:** Corresponding H&E section of Desmoid Type Fibromatosis Breast showing long sweeping fascicles of bland spindle cells aligned parallel to one another. The fascicles were variably cellular with an infiltrative margin and absence of any epithelial neoplastic component. Background showed inflammatory infiltrate.(H&E 10x and 20x);

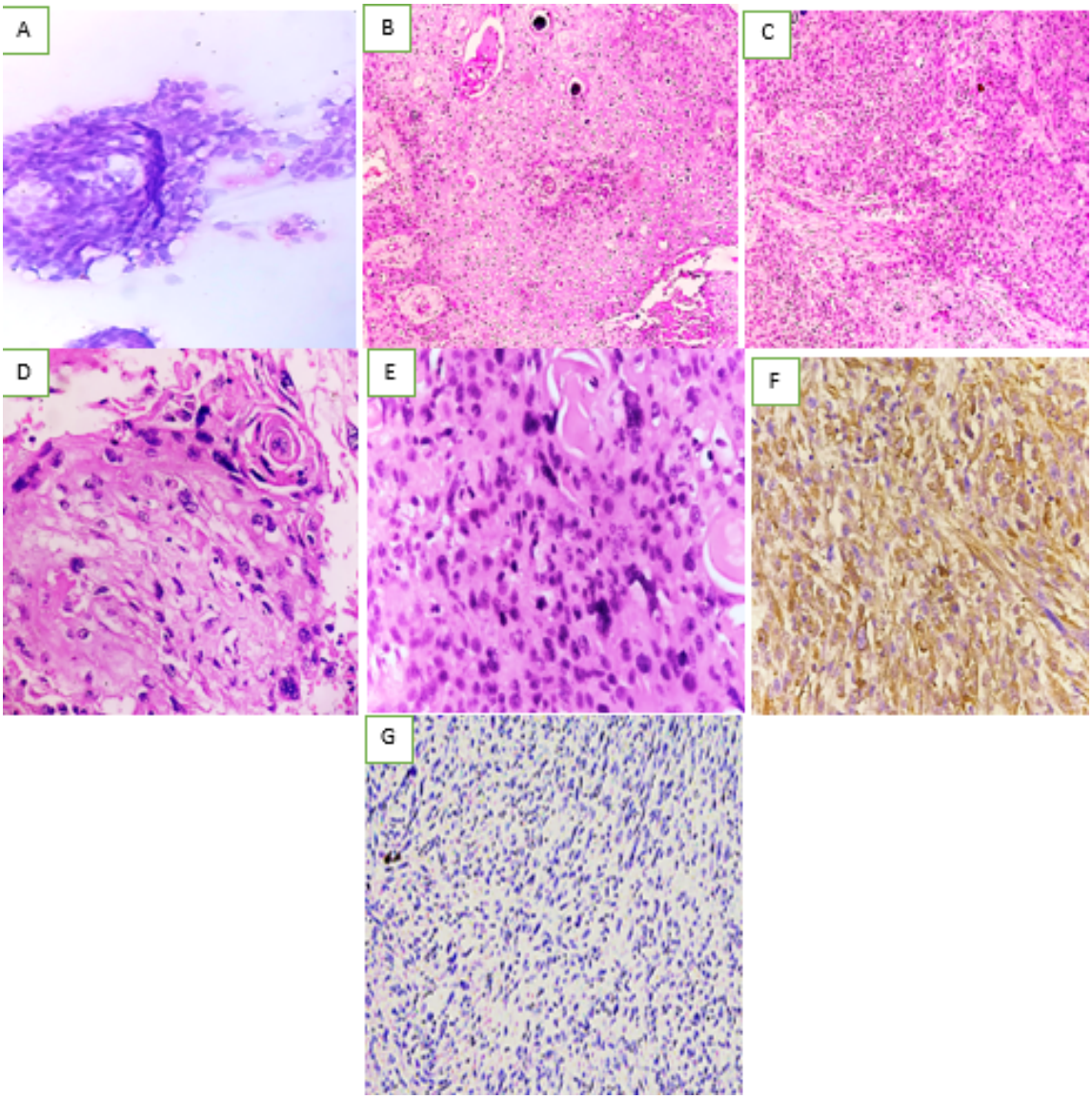

Figure 7: A: FNA smear of Metaplastic Carcinoma of Breast showing sheet of pleomorphic spindle cells in a myxoid background. (H&E 40 x); **B,C:** Metaplastic Carcinoma corresponding section from tumor area showing proliferation of atypical spindle cells with moderate cytological atypia, coarse granular chromatin with prominent nucleoli and eosinophilic cytoplasm with interlacing trabeculae of osteoid differentiation. (H&E 20x); **D,E:** H&E section Metaplastic Carcinoma of Breast showing atypical spindle cells in a myxoid background along with osseous differentiation, areas of necrosis and mitosis of 5-10/10hpf. (H&E 40x); **F,G :** Metaplastic Carcinoma Vimentin positive and focally CYTOKERATIN positive in malignant spindle cell. (IHC 40x and 20 x)

panel was applied in 105 selected cases using VENTANA BENCHMARK XT in which a corroboration in the diagnosis made before and after applying IHC was found in 85 cases (81%) and in 15 cases (14.3%) the histopathological diagnosis changed after application of IHC while in 5 cases (4.7%) no final diagnosis was made (Table 9).

Out of 105 cases, the diagnosis got changed after application of IHC in 20 cases. Among these 20 cases, there were 10 cases in which diagnosis of metaplastic Carcinoma/malignant phyllodes were made on HPE but after application of CD34 and other IHC markers the lesion was confirmed as malignant phyllodes tumor (Table 9). In Another 5 cases of spindle cell lesion where a differential diagnosis was made as desmoid type fibromatosis/solitary fibrous tumor. We applied STAT 6, Beta catenin and SMA, result of IHC came out to be positive for SMA and Beta catenin and Negative for STAT 6 hence final diagnosis after application of IHC was the desmoid type fibromatosis of breast was made. In rest 5 cases no conclusion

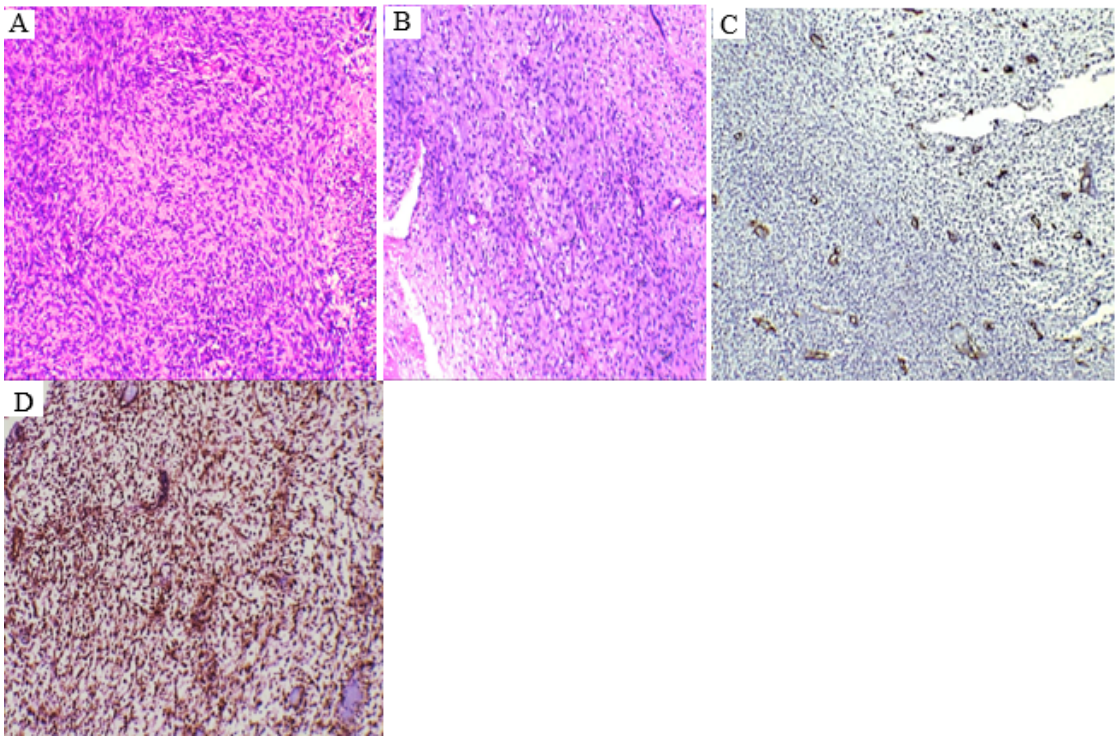

Figure 8: A,B : Myxofibrosarcoma of Breast Corresponding H& E section showing pleomorphic spindle shaped cells with pseudo lipoblasts and condensation of cells around vessels. (H&E 20x); **C,D:** Myxofibrosarcoma of Breast CD34 - Cytoplasmic Positivity (IHC X 10x) and SMA - Diffuse strong cytoplasmic positivity. (IHC 20x)

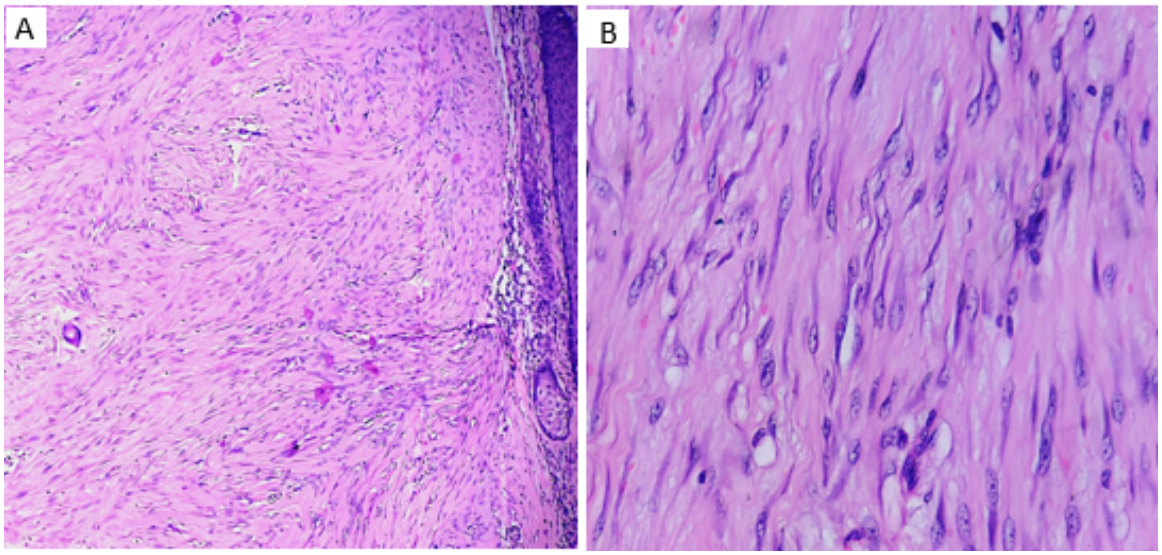

Figure 9: A,B: H&E sections of Neurofibroma Breast showing benign appearing spindle cells arranged in form of bundles and fascicles with intervening collagen. (H&E 20x, and 40x)

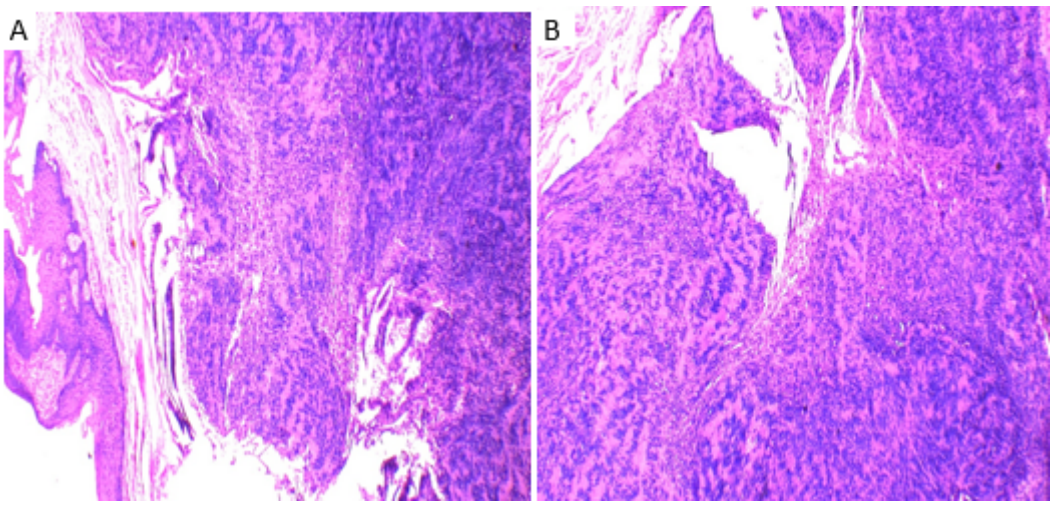

Figure 10: A,B: H&E of Schwannoma of Breast showing two architectural patterns in variable proportions: Antoni A areas composed of compact, elongated cells with nuclear palisading (Verocay bodies) and Antoni B areas is less cellular. The tumor area composed of densely packed spindled cells arranged in intersecting fascicles along with hyalinized blood vessels and variable lymphoid aggregates. (H&E 20x)

Table 2: Distribution of Spindle cell lesions of breast according to cytological diagnosis (n= 105) andhistopathological diagnosis (n=220).

Type	Number of cases	Percentage
	Cytological Diagnosis (n=105)	
Benign spindle cell lesions	70 (In 49 cases histopathological diagnosis was available)	66.7%
Malignant Spindle cell lesions	25 (In 11 cases histopathological diagnosis was available)	23.8%
Inconclusive	10	9.5%
TOTAL	105	100
Histopathological diagnosis (n=220)		
Benign Spindle cell lesions	148	67.3%
Borderline or Low grade malignant spindle cell lesions	30	13.6%
Spindle cell malignancy	42	19.1%
Total	220	100

Table 3: Distribution of cytological cases according to Age (n= 105).

Age in Years	Benign spindleCell lesions	Malignant spindleCell lesions	Inconclusive	Total (%)
<20	02(1.9%)	0	0	02(1.9%)
20-29	02(1.9%)	01(0.9%)	2(1.9%)	05(4.7%)
30-39	22(21%)	02(1.9%)	06(5.7%)	30(28.6%)
40-49	35(33.3%)	15(14.3%)	02(1.9%)	52(49.5%)
50-59	06(5.7%)	03(2.9%)	0	09(8.6%)
≥60	03(2.9%)	04(3.8%)	0	07(6.7%)
Total	70(66.7%)	25(23.8%)	10(9.5%)	105(100%)

Table 4: Distribution ofcytologically diagnosed spindle cell lesions of breast (n=105).

TYPE		No of cases	Percentage
Spindle cell lesion of breast favoring	• Benign lesion	40	38%
	• Malignant lesion	25	24%
Benign Phyllodes tumor		30	28.5%
Inconclusive		10	9.5%
Total		105	100%

Table 5: Distribution of histopathological cases according to age (n=220).

Age in years	Benign	Borderline Malignant	Malignant	Total
<20	13(5.9%)	00	00	13(5.9%)
20-29	25(11.3%)	02(0.9%)	01(0.4%)	28(12.7%)
30-39	40(18.1%)	06(2.7%)	05(2.2%)	51(23.1%)
40-49	55(25%)	08(3.6%)	11(5%)	74(33.6%)
50-59	10(4.54%)	09(4.1%)	20(9.1%)	39(17.7%)
≥60	05(2.2%)	05(2.2%)	05(2.2%)	15(6.8%)
Total	148	30(13.6%)	42(19.1%)	220(100%)

Table 6: Subtypes of spindle cell lesions of breast diagnosed according tohistomorphological features (n=220)

Histopathological diagnosis	No. of cases	Percentage
Benign phyllodes tumor	85	38.6%
Borderline phyllodes tumor	30	13.7%
Malignant phyllodes tumor	25	11.4%
PASH	15	6.8%
Metaplastic carcinoma	13	6%
Myofibroblastoma	13	6%
Nodular Fasciitis	12	5.4%
Desmoid type Fibromatosis	10	4.54%
Inflammatory Myofibroblastic Tumor	04	1.81%
Neurofibroma	03	1.36%
Schwannoma	03	1.36%
Myxofibrosarcoma	03	1.36%
DFSP	02	0.9%
Spindle cell lipoma	02	0.9%
Total	220	100%

Table 7: Cyto-histopathological correlation (n=60)

Diagnosis on FNAC (n = number of cases)	Diagnosis on Histopathology (n = number of cases)	Concordant Cases (%)	Discordant cases (%)
Spindle cell lesion favoring benign Phyllodes tumor (n=20)	• Benign phyllodes tumor on histopathology except for 1 case i.e; Malignant phyllodes tumor was made as the final diagnosis	19(31.6%)	1(1.7%)
Benign spindle cell lesions of breast (Not otherwise specified) (n=30)	• Benign Phyllodes tumor (n=17) • PASH(n=4) • Myofibroblastoma (n=3) • Nodular Fasciitis (n=2) • Fibromatosis(n=1) • Neurofibroma(n=1) • Schwannoma (n=1) • Spindle cell lipoma(n=1)	30(50%)	0
Spindle cell malignancy favouring malignant phyllodes tumor (n = 1)	• Benign phyllodes tumor(n=1)	0	1(1.7%)
Malignant spindle cell lesion of breast (n=9)	• Malignant phyllodes tumor(n=5) • Metaplastic spindle cell carcinoma (n=3) • Myxofibrosarcoma (n=1)	9(15%)	0
Total cases = 60(100%)		58(96.6%)	02(3.4%)

Table 8: Showing sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy of FNAC in diagnosing spindle cell tumors of breast.

Diagnosis on Cytology	Diagnosis on Histopathology	No. of cases (n=60)
Benign	Benign	49
Malignant	Malignant	09
Benign	Malignant	01
Malignant	Benign	01
Sensitivity	98%	
Specificity	90%	
Accuracy	96.67%	
PPV	98%	
NPV	90%	

was made due to overlapping histomorphological and immunohistochemical features.

4. Discussion

Based on the spectrum of differentiation, morphological, immunohistochemical and molecular characteristics, WHO, 2019 has categorised breast lesions and tumors into various subtypes. With varying tumor characteristics, spindle cell tumors represent a different category of breast lesions.[8] An algorithmic approach is suggested for the diagnosis of different entities and the following parameters should be clearly evaluated: (1) cellular structures, (2) existence and degree of atypia, (3) growth pattern, (4) mitotic figures, (5) clinical and radiological characteristics.[9,10]

The main objective of this study was to analyse benign and malignant spindle cell lesions and tumors of the breast in terms of clinical profile and to ascertain a cytopathological and histopathological correlation with special emphasis on cyto-histomorphological and immunohistochemical characteristics of these lesions.

Our study was a 5 year retrospective and prospective study of 260 patients that were diagnosed with a breast spindle cell lesion or a neoplasm. Fine needle aspiration cytology was performed and as per routine laboratory protocol, the surgically resected specimens and biopsies were processed. Various basic immunohistochemical markers such as broad spectrum Cytokeratins, S100, CD34, SMA, Desmin, Vimentin and Ki-67 were applied as per the need of the case. Whenever required, lineage specific or specific IHC markers were used to arrive at a final diagnosis.

In our study, the age of presentation for spindle neoplasms in the breast exhibited a broad spectrum, ranging from under 20 to over 60 years. Notably, the 40-49 age group emerged as the most common age range, with 48.46% of cases falling into this category. This age trend is consistent with previous research by Unal et al. in (2015),[11] as well as studies by Abd El All[12] and Lekshmi et al,[13] which reported median ages of 46.2 and 50.37 years, respectively, for spindle cell breast lesions. Benign tumors were predominantly observed in the 40-49 age group in our study, with only 3% occurring in individuals aged 60 and above. Conversely, malignant spindle cell neoplasms primarily affected patients between 40-49 years, constituting 10% of cases. Notably, the lowest incidence of malignant spindle cell neoplasms was observed in individuals under 30 years of age, accounting for less than 1% of total spindle cell malignancies. These findings closely align with the observations made by Lakhani et al. (2012),[8] who noted that malignant metaplastic carcinomas are more frequently diagnosed in patients over the age of 50. This reinforces the importance of age-related considerations in understanding and managing spindle neoplasms of the breast.

The vast majority of patients (92.3%) in our study reported the presence of a palpable lump or mass in the breast as their primary complaint. This observation is in line with the findings of Ünal et al. in (2015),[11] where palpable masses were the predominant complaint, and only patients with Angiosarcoma reported pain. A retrospective study by Blanco et al in (1999)[14] further supported our results, with all patients presenting with palpable breast lumps of varying sizes. Additionally, our study identified other complaints, such as mastalgia (pain) in 40% of cases, lymphadenopathy in 30.7%, ulceration or fungating mass in 20.7%, nipple discharge in 16.1%, and nipple retraction in 7.6% of cases. These findings highlight the diverse clinical presentations of breast spindle cell neoplasms, with Lekshmi et al (2017)[13] noting that the majority of cases present as painless masses, while one-third of cases report pain.

In our study, we analysed a total of 220 histopathological cases, comprising 190 resected lumpectomy/mastectomy specimens and 30 small/core needle biopsies. The spindle cell tumors were categorized into three main groups, with 148 cases classified as benign tumors, 42 as malignant tumors, and 30 as atypical/borderline tumors. Notably, our findings revealed a higher prevalence of benign tumors compared to malignant ones. This pattern is consistent with the observations made by Abd El all in 2006, further underscoring the predominance of benign spindle cell neoplasms in both studies.[12] Understanding the distribution of these tumor types is crucial for accurate diagnosis and

Table 9: DifferentImmunohistochemical (IHC) stains applied

Histopathological diagnosis(n=105)	Immunohistochemical (IHC) markers	Result	Final Diagnosis after IHC Application
Benign phyllodes tumor (n=45)	CD34 & Vimentin CK*	Positive	Benign phyllodes tumor (n=44)
	EMA SMA,	Negative	
	DESMIN S100	Negative	
	CD45	Negative	
	CD117	Negative	
	CD31	2-6%	
	p63 Ki67		
Malignant phyllodes tumor (n=12)	CD34 & Vimentin CK*	Positive/Focal Ly	Malignant phyllodes tumor (n=10)
	EMA SMA	Positive	
	Desmin S100	Negative	
	CD45 CD117	Negative	
	CD31	Negative	
	p63	Negative	
	Ki67	15-30%	
Malignant phyllodes tumor VS Metaplastic carcinoma (n=10)	CD34 & Vimentin CK*	Positive	Malignant phyllodes tumor (n=10)
	EMA SMA	Negative	
	DESMIN S100	Negative	
	CD45	Negative	
	CD117	Negative	
	CD31	15-30%	
	p63 Ki67		
Metaplastic carcinoma (n=5)	Vimentin CK*	Positive	Metaplastic carcinoma (n=4)
	CD34 S100	Positive	
	P63 &CK 5/6	Negative	
		Negative	
Myxofibrosarcoma (n=1)		Positive	Myxofibrosarcoma (n=1)
	SMA CD34 S100	Positive	
	DESMIN& CK*	Positive	
		Negative	
		Negative	
Dermatofibrosarco ma protuberance (DFSP) (n=1)	CD34 Vimentin S100	Positive	Dermatofibrosarco ma protuberance (DFSP) (n=1)
		Positive	
		Negative	
Fibromatosis VS Solitary fibrous tumor (n=5)	Beta catenin SMA S100	Positive	Fibromatosis (n=5)
	STAT6 Ki-67	Positive	
		Negative	
		Negative	
		<5%	
Nodular Fasciitis (n=6)	SMA S00 DESMIN	Positive	Nodular Fasciitis (n=5)
	CD34	Negative	
		Negative	
		Negative	
PASH (n=6)	CD34 DESMIN	Positive	PASH (n=6)
		Focally	
	CK* & CD31	Positive	
		Negative	
Myofibroblastoma (n=9)	SMA	Positive	Myofibroblastoma (n=9)
	Vimentin	Positive	
	CK*	Negative	
	S 100	Negative	
	Desmin	Focally	
Neurofibroma (n=1)	S100	+Ve/Negative	Neurofibroma (n=1)
	CD34	Positive	
Schwannoma (n=1)	S100	Positive	Schwannoma (n=1)
	CD34	Positive	
		Negative	
Inflammatory myofibroblastic tumor (n=2)	Beta catenin ALK 1	Negative	Inflammatory myofibroblastic tumor (n=2)
		Positive	
Spindle cell Lipoma (n=1)	CD34 & Vimentin S100	Positive	Spindle cell lipoma (n=1)
		Positive in Fat Cells	

*AE1/AE3 and CAM5.2

effective treatment strategies.

Within our study, Phyllodes tumors were the most prevalent, accounting for 63.63% of all cases. This category included 38.36% of benign Phyllodes tumors, 13.6% of borderline Phyllodes tumors, and 11.36% of malignant Phyllodes tumors (Figures 2 and 3). Our findings align with Tan et al.'s (2016)[15] study, where Phyllodes tumors were graded as benign, borderline, or malignant based on histomorphological characteristics. Additionally, research by Chaney et al (2000).[16] Cheng et al., (2006)[17] & WHO (2019),[7] respectively, also supported our observations, showing that benign Phyllodes tumors were the most frequent, accounting for a significant portion of cases, while borderline and malignant Phyllodes tumors constituted smaller proportions. This consistency underscores the prevalence of benign Phyllodes tumors in our study and in the broader literature.

Mesenchymal tumors were the second most common subgroup in our study comprising a total of 67 cases (30.45%). In our study, myofibroblastoma exhibited characteristic microscopic features, with tumor cells arranged in intersecting fascicles of spindle-shaped cells separated by collagen bands. Immunohistochemistry revealed positivity for SMA and Vimentin, while Pan cytokeratin and S100 were negative (Figure 4). These findings closely align with the observations of Magro et al in 2018, underscoring the consistency in the histopathological and immunohistochemical characteristics of myofibroblastoma.[18]

Cases of Nodular fasciitis on cytology showed plump fibroblasts with pale cytoplasm, uniform vesicular nuclei and small nucleoli in addition to infrequent giant cells and other inflammatory cells which was in accordance with a study by Michelow et al., 2019.[5] H&E sections showed spindle to oval cells arranged in short fascicles along with Extravasated erythrocytes and scattered lymphocytes (Figure 5). On applying IHC SMA was positive which was similar with the study of Rakha et al., 2016.[5]

Rakha et al (2016) and Michleow et al (2019) reported that fibromatosis of the breast accounted for 0.2% of primary breast lesions, which closely matches our findings of 0.1% of total breast lesions.[5,6] The age range of patients with mammary fibromatosis in their studies, spanning from 13 to 80 years with a median age of 25 years, aligned with our observations. In our study, cases of Desmoid type Fibromatosis exhibited characteristic features on FNAC, including bland spindle cells in a hypocellular stromal background. Histopathologically, the lesion comprised fascicles of spindle cells and lymphocytes at the lesion edge (Figure 6). Immunohistochemistry results showed positive staining for β-catenin and SMA, while CD34 was negative, consistent with the findings of Lee et al. (2007).[19] These similarities highlight the diagnostic consistency of fibromatosis across studies.

In our study, cases of metaplastic breast carcinoma exhibited cellular FNAC smears with pleomorphic spindle cells showing increased N: C ratio, hyperchromasia, and high mitotic activity. Osseous differentiation was observed in the background, along with necrotic and myxoid areas in some cases. The cytological diagnosis was malignant spindle cell lesion, warranting further histopathological examination. Histologically, we observed atypical spindle cells with prominent nucleoli, eosinophilic cytoplasm, and osteoid differentiation in 5 cases (Figure 7). Similar findings were reported by Charu et al. (2017),[3] showing atypical nuclei in spindle cells and high mitotic activity on FNAC, along with pleomorphic cells histologically. Abd El All (2006)[12] noted Vimentin, CK, SMA, S100, and CD10 positivity in spindle cells and negative Desmin and CD34. Our study exhibited comparable findings with Vimentin, CK5/6, and p63 positivity, focal Pan Ck positivity, and negativity for CD34, S100, CD117, SMA, Desmin, with a high Ki-67 index. These consistent features emphasize the diagnostic and immunohistochemical characteristics of metaplastic breast carcinoma.

The FNA of a myxofibrosarcoma revealed variable cellularity with a myxoid granular background. Tumor cells were large, with round to spindled shapes and nuclear pleomorphism. H&E staining showed pleomorphic spindle-shaped cells with pseudo lipoblasts and a curvilinear arrangement around vessels (Figure 8). Immunohistochemistry with SMA and CD34 displayed strong cytoplasmic positivity, while Ki67 was high and S100, Desmin were negative, consistent with Klopčič et al. (2009).[20]

Among tumors of neural origin, in our study we encountered a total of 6 cases of Schwannoma and Neurofibroma, collectively accounting for less than 1% of primary breast tumors. These findings closely align with Hasebe et al.'s study in Japan, where neurilemmomas accounted for only 0.2% of benign intra-mammary tumors.[21] On FNAC, both Schwannoma and Neurofibroma exhibited elongated, bland spindle cells with pointed ends and indistinct cytoplasm (Figures 9 and 10), consistent with the observations of Bellezza et al in 2007[22] and Soni et al in 2014.[23] These consistent features emphasize the rare but characteristic histopathological patterns of these neural tumors in the breast.

4.1. Efficacy of cytopathology in diagnosing spindle cell lesions of breast

Out of 15,270 cases of breast lesions analysed over a 5-year period, 105 cases (0.6%) were diagnosed as spindle cell lesions/neoplasms of the breast on cytology, consistent with Chhieng et al.'s findings of <1% in breast FNAC.[24] Bardales et al. (1995)[25] also reported a similar rate of 0.13% in their sample of 5,500 breast lesions, aligning with our results. Mukhopadhyay et al. (2017)[26] reported that benign spindle

cell lesions were most prevalent in the 3rd and 4th decades, consistent with our study's findings. In our study, malignant lesions were primarily observed in the 4th decade, whereas in their study, they were more common in the 5th and 6th decades.

4.2. Comparative analysis and correlation of cytological and histopathological diagnoses

Among 65 cases with FNAC followed by histopathology, 49 benign and 9 malignant cases were correctly diagnosed on cytology. There was one false positive and one false negative case. Of the correctly diagnosed benign cases, 19 were benign phyllodes tumors, while 30 were initially categorized as benign spindle cell lesions on cytology but further subtyped as benign phyllodes tumor, PASH, Myofibroblastoma, Nodular Fasciitis, Fibromatosis, Neurofibroma, Schwannoma, and Spindle cell lipoma on histopathology.

Among the correctly diagnosed malignant cases, 9 were initially diagnosed as malignant spindle cell lesions on cytology, which were subsequently subtyped as Metaplastic spindle cell carcinoma, Malignant phyllode tumor, and Myxofibrosarcoma on histopathology.

Discrepancies in two cases were noted, with one initially diagnosed as malignant phyllodes tumor on cytology later reclassified as benign phyllodes tumor on histopathology. The other case initially labeled as benign phyllodes tumor on cytology was reclassified as malignant phyllodes tumor on histopathology due to infiltrating growth, stromal overgrowth, nuclear changes, and a high mitotic count.

Mukhopadhyay et al. (2017)[26] found FNAC useful in distinguishing benign from malignant spindle cell lesions but challenging in exact categorization, particularly for specific subtyping of malignant lesions due to overlapping cytological features. Well-differentiated malignant lesions and those with distinct benign features were easier to diagnose and subtype.

So the following inference was made:

Sensitivity = 98%

Specificity = 90%

Positive predictive value = 98%

Negative predictive value = 90%

Diagnostic accuracy of FNAC = 96.67%

These results were comparable with most of the published studies. (Table 7).

Therefore, the present study concluded that FNAC can be used with reasonable sensitivity, specificity and accuracy as a reliable diagnostic tool for preoperative triaging of benign and malignant spindle cell lesions, although a particular diagnosis may be difficult. This is where immunohistochemistry plays its part. The explanations for such a wide variety of variable outcomes are multi factorial, with the lack of FNA on-site service and collaboration between surgeons, radiologists and pathologists being the key factors.

4.3. Immunohistochemistry effectiveness in diagnosing spindle cell lesions of breast

Among the 105 cases, the diagnosis changed in 20 cases after applying IHC. In 10 of these cases initially diagnosed as metaplastic carcinoma or malignant phyllodes tumors, IHC confirmed them as malignant phyllodes tumors. In 5 cases with a differential diagnosis of desmoid type fibromatosis/solitary fibrous tumor, IHC revealed positivity for SMA and Beta catenin, resulting in a final diagnosis of desmoid type fibromatosis of the breast. In the remaining 5 cases, overlapping histomorphological and immunohistochemical features prevented a conclusive diagnosis.

In our study, benign and borderline phyllodes tumors were positive for CD34 and Vimentin, while Ck, EMA, SMA, DESMIN, S100, CD45, CD117, CD31, and p63 were negative, aligning with Dunne et al.'s findings in 2003.[27] Out of 13 cases of Myofibroblastoma, 9 showed positivity for SMA and Vimentin, while Cks (AE1/AE3, CAM 5.2), S100, and Desmin were negative, which is consistent with the observations made by Bayrak et al. in 2019.[28]

Schwannoma and Neurofibroma were consistently positive for S100 in all cases, aligning with Rakha et al.'s study in 2016.[6]

In 5 cases of metaplastic carcinoma, 4 showed Vimentin positivity and focal positivity for CK, while 2 cases were negative for CK. This is consistent with Dunne et al.'s findings in 2003,[27] where CK staining in metaplastic spindle cell carcinoma could be heterogeneous, and 34 Beta E12 was the most frequently expressed CK in sarcomatoid areas of metaplastic spindle cell carcinomas.

In conclusion, a systematic approach should be used for spindle cell lesions, considering cytomorphology as the initial step. An algorithmic diagnosis should evaluate cell structure, atypia, growth pattern, mitotic activity, immunohistochemistry, and clinical/radiological features. To achieve a conclusive diagnosis, it's essential to assess clinico-radiological, cytomorphological, and histomorphological features, create a differential diagnosis, and classify the tumor as benign or malignant. However, subtyping by histomorphology alone is often insufficient, and ancillary testing is required to confirm histogenesis and reach a definitive diagnosis.

5. Conclusion

Spindle cell lesions in the breast are relatively rare, accounting for only 1.7% of cases. Diagnosing them through histopathology alone can be challenging due to morphological overlap. A comprehensive approach that considers clinical characteristics, cyto-histological parameters, and immunohistochemistry is essential for

accurate diagnosis, risk assessment, and treatment planning. While defining features may not be present for each entity, a practical diagnostic algorithm that stratifies these lesions and employs a targeted immunohistochemical panel is crucial. In some cases, molecular and genetics studies may also be necessary to guide treatment decisions in recent years.

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7. Conflict of Interest

None.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2021;71(3):209–49.
2. Malvia S, Bagadi SA, Dubey US, Saxena S. Epidemiology of breast cancer in Indian women. *Asia Pac J Clin Oncol*. 2017;13(4):289–95.
3. Charu V, Cimino-Mathews A. Spindle-cell lesions of the breast. *AJSP: Rev Rep*. 2017;22:116–23.
4. Naso JR, Chiu CG, Goecke ME, Chang D, Shiau CJ. Benign spindle cell lesions of the breast: a diagnostic approach to solitary fibrous tumor, nodular pseudoangiomatous stromal hyperplasia and nodular fasciitis. *J Clin Pathol*. 2019;72(6):438–42.
5. Michelow PM, Field AS. Spindle cell lesions of the breast on fine-needle aspiration biopsy: a Miscellany of masses. *Acta Cytol*. 2019;63(4):328–39.
6. Rakha EA, Aleskandarany MA, Lee AH, Ellis IO. An approach to the diagnosis of spindle cell lesions of the breast. *Histopathology*. 2016;68(1):33–44.
7. Lokuhetty D, White VA, Watanable R, Cree IA. World Health Organisation Classification of Tumors. In: Breast Tumors. 5th Edn. Lyon, France: International Agency for Research on Cancer (IARC) Press; 2019. p. 8–10.
8. Lakhani SR, Ellis IO, Schnitt SJ, Tan PH, Van De Vijver M. World Health Organization classification of tumours. WHO classification of tumors in the breast; 2012.
9. Al-Nafussi A. Spindle cell tumours of the breast: practical approach to diagnosis. *Histopathology*. 1999;35(1):1–13.
10. Varma S, Shin SJ. An Algorithmic Approach to Spindle Cell Lesions of the Breast. *Adv Anatomic Pathol*. 2013;20(2):95–109.
11. Ünal B, Erdoğan G, Karaveli F. Step by step approach to rare breast lesions containing spindle cells. *Springerplus*. 2015;4:678. doi:10.1186/s40064-015-1480-y.
12. All HAE. Breast spindle cell tumours: about eight cases. *Diagn Pathol*. 2006;1:1–13. doi:10.1186/1746-1596-1-13.
13. Lekshmi D, Cicy P, Sansho E, Deepa S, Laila R. Spindle cell lesions of breast: a retrospective analysis with emphasis on diagnostic challenges. *Int J Adv Med*. 2017;4(6):1627. doi:10.18203/2349-3933.ijam20175179.
14. Blanco AJ, Serrano BV, Romero RR, Cendejas EM. Phyllodes tumors of the breast. *Eur Radiol*. 1999;9(2):356–60.
15. Tan BY, Acs G, Apple SK, Badve S, Bleiweiss IJ, Brogi E, et al. Phyllodes tumours of the breast: a consensus review. *Histopathology*. 2016;68(1):5–21.
16. Chaney AW, Pollack A, Mcneese MD, Zagars GK, Pisters PW, Pollock RE, et al. Primary treatment of cystosarcoma phyllodes of the breast. *Cancer*. 2000;89(7):1502–11.
17. Cheng SP, Chang YC, Liu TP, Lee JJ, Tzen CY, Liu CL, et al. Phyllodes tumor of the breast: the challenge persists. *World J Surg*. 2006;30(8):1414–21.
18. Magro G. Differential diagnosis of benign spindle cell lesions. *Surg Pathol Clin*. 2018;11(1):91–121.
19. Lee AH, Hodi Z, Ellis IO, Elston CW. Histological features useful in the distinction of phyllodes tumour and fibroadenoma on needle core biopsy of the breast. *Histopathology*. 2007;51(3):336–44.
20. Klopčičc U, Lamovec J, Luzar B. Fine needle aspiration biopsy of primary breast myxofibrosarcoma: a case report. *Acta Cytol*. 2009;53(1):109–12.
21. Hasebe T. Pathology of benign breast diseases. *Pathol Clin*. 1989;7:440–8.
22. Bellezza G, Lombardi T, Panzarola P, Sidoni A, Cavaliere A, Giansanti M, et al. Schwannoma of the breast: a case report and review of the literature. *Tumori J*. 2007;93(3):308–11.
23. Soni PB, Verma AK, Chandoke RK, Nigam JS. A prospective study of soft tissue tumors histocytopathology correlation. *Patholog Res Int*. 2014;p. 678628. doi:10.1155/2014/678628.
24. Chhieng DC, Cangiarella JF, Waisman J, Fernandez G, Cohen JM. Fine- needle aspiration cytology of spindle cell lesions of the breast. *Cancer*. 1999;87(6):359–71.
25. Bardales RH, Stanley MW. Benign spindle and inflammatory lesions of the breast: diagnosis by fine-needle aspiration. *Diagn Cytopathol*. 1995;12(2):126–30.
26. Mukhopadhyay A, Naskar S, Dey R, Basu K. Female breast lesions–a five year study in a tertiary care centre. *Int J Anat Radiol Surg*. 2017;6(1):10–4.
27. Dunne B, Lee AH, Pinder SE, Bell JA, Ellis IO. An immunohistochemical study of metaplastic spindle cell carcinoma, phyllodes tumor and fibromatosis of the breast. *Hum Pathol*. 2003;34(10):1009–15.
28. Bayrak BY, Eruyar AT, Güneş A. Cyto-Histopathological Findings of Myofibroblastoma of the Breast: A Case Report. *Istanbul Med J*. 2019;20(2):148–51.

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