



## Original Research Article

## Phyllodes tumors of breast: An experience in a tertiary care centre

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## ABSTRACT

Phyllodes tumors are uncommon fibroepithelial tumors of breast that have potential for recurrence and metastasis. Triple assessment by clinical, radiological and histological examination forms the fundamental basis for the evaluation of phyllodes tumor. Treatment could be either by wide excision or mastectomy provided that clear histological margins are achieved. Wide local excision with at least 1 cm clear margin is currently the standard of treatment of phyllodes tumor in most institutions. Most of these behave in benign fashion however, malignant tumors have higher tendency for local recurrence and systemic dissemination to lungs, brain. Lymph node involvement is rare.

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## 1. Introduction

Phyllodes tumors are rare biphasic tumors exclusively & uniquely occurring in breast tissue.<sup>1,2</sup> Clinically, they resemble fibroadenoma. Based on histological features they are classified into benign, borderline and malignant. Because of their diverse biological behaviour, they have tendency to recur and can progress to malignancy. Benign phyllodes tumor may show spectrum of histological features like hyperplasia, metaplasia, dysplasia, in situ and even invasive ductal malignancies. It is also known to occur synchronously with fibroadenoma. Malignant tumors may show heterologous differentiation and should be differentiated from primary sarcomas. Rarely involvement of the axillary lymph nodes occurs. We present ten case series of phyllodes tumors, few with unusual clinical and histological features observed in 10% of our patients.

## 2. Aims and Objectives

1. To study and analyse the clinical and histopathological features for diagnosis of phyllodes tumor.

2. To emphasize the need of extensively sampling for accurate histopathological diagnosis to prevent recurrence.

## 3. Materials and Methods

This retrospective study was conducted on ten phyllodes tumor patients diagnosed during the period of 2012 to 2017 patients in the department of pathology. Clinical data and histopathological slides of each cases were retrieved and analysed.

## 4. Results

All patients were female with the mean age of 45 years. The youngest age was 21 years old and the eldest was 86 years old. Patients presented with painless mass of few months to two years duration. Pre-operative diagnosis by FNAC was done in five of them and reported as cellular fibroadenoma. One had undergone biopsy with inconclusive result. Unilateral involvement of breast was common, with bilateral involvement in two patients. USG and mammography was not done in majority of patients. The unusual clinical features were presence of synchronous

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fibroadenoma in the same breast and the other in the contralateral breast. All the ten cases of phyllodes tumors were diagnosed histologically by following WHO criteria into benign (60%), borderline (10%) and malignant (30%). Histologically, type of margins, stromal cellularity, atypia and mitosis were assessed. Extensive sclerosis and myxoid change were seen in the stroma of benign tumors. Malignant tumor revealed more than 10 mitosis per high field 10% showed tumor necrosis. All tumors had one cm free surgical margin excised. The average tumor size was 8cm in benign and 20 cm in malignant tumors. Out of three malignant tumors, one presented with lymph node metastases while two also had recurrence of the tumor (20%). Pre-operative diagnosis was done by USG (Birads IV) in this metastatic tumor. However, FNAC performed was inconclusive. Tumors were assessed clinically by size into benign tumors and had undergone simple mastectomy with or without axillary clearance. Out of the three malignant tumors, one was treated by modified radical mastectomy and presented with recurrence after two months. However, patients with benign tumor (60%) had no recurrence.

## 5. Discussion

Phyllodes tumors are relatively rare lesions, accounting for 0.4–1% of all breast tumors.<sup>1–3</sup> The term cystosarcoma phyllodes was first coined by Johannes Muller in 1838 and was believed to be benign when Ackerman in 1981 reported the malignant potential behaviour of this tumor.<sup>1,2</sup> It was then adopted by WHO as phyllodes tumor and based on histomorphological criteria, Rosen subclassified them into benign, borderline & malignant tumors. Table 1. The biphasic pattern, namely the epithelial and stromal component differentiates it from other primary tumor like sarcomas. Most of the tumors are benign (35% to 64%) while rest are borderline and malignant sub types.<sup>3,4</sup>

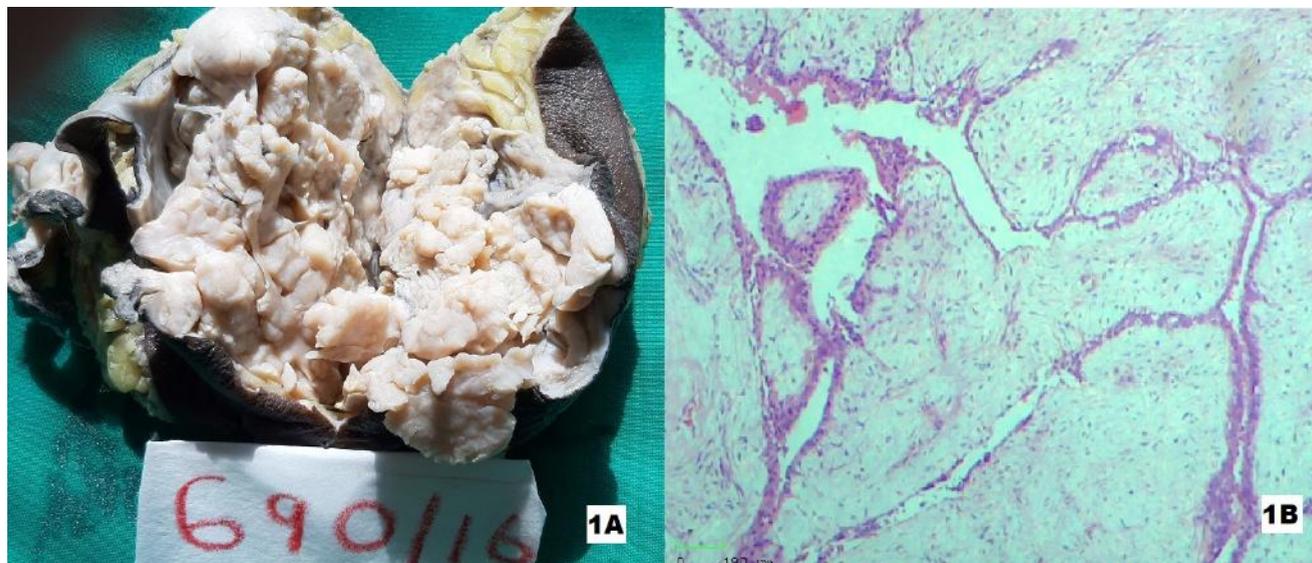
Clinical, radiological and histological examination forms the fundamental basis for the evaluation of phyllodes tumors. Since these tumors have a wide spectrum of clinical and morphological features they may pose difficulties in pre-operative diagnosis.<sup>5</sup> In our study preoperative FNAC was the common diagnostic modality and basis for deciding the type of surgery. Patients diagnosed as fibroadenoma on FNAC with tumor size of less than 10cm were treated with lumpectomy. Majority did not undergo USG/mammography. One case with axillary lymph node involvement was diagnosed as malignant on USG (Birads IV). The existing diagnostic modalities, USG, MRI or X-ray may not differentiate these tumors. USG is convenient and non invasive hence preferred choice of investigation and reveals as a bulky lobulated mass, with clear boundaries, internally mainly solid hypoechoic uneven echoes, potentially with scattered echo-free zones. Malignant phyllodes tumor does not follow the general rules of other types of breast cancer in terms of echo attenuation,

and micro calcification is common. Fine needle aspiration (FNA) and core needle biopsy (CNB) is the pathology basis for preoperative diagnosis.<sup>6</sup> However, due to the location and coverage limits on the amount drawn, it is difficult to differentiate with epithelial neoplasms, or other type of fibroadenoma. Therefore, the diagnostic accuracy of phyllodes tumor is low. Most studies suggest that the diagnosis accuracy rate of FNA or CNB for breast phyllodes tumor is about 50%. One of the study by Efares B et al.<sup>3</sup> reported that the core needle biopsy has a good diagnostic sensitivity compared to definitive diagnosis on surgical specimen.

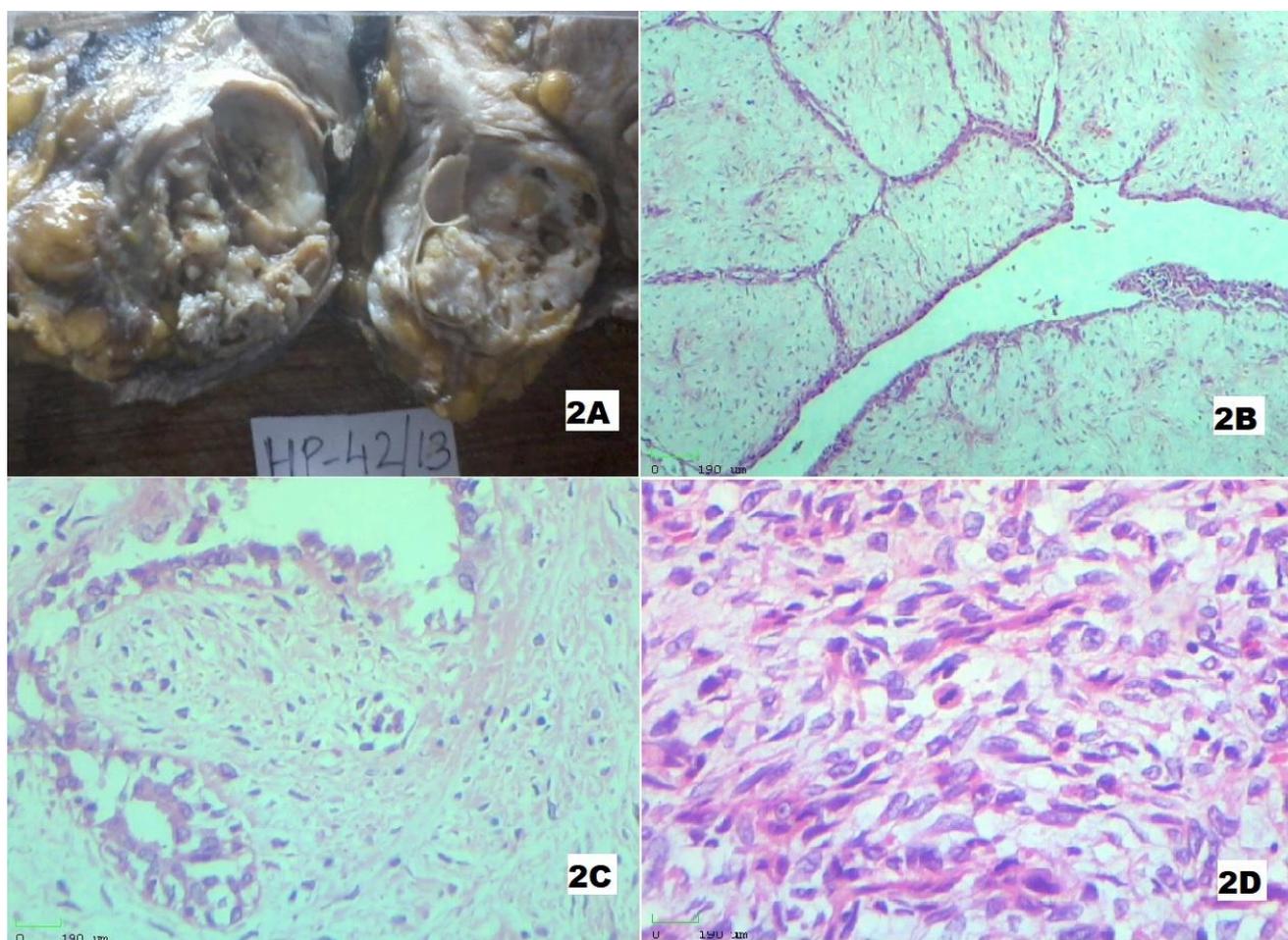
Our series describe the experience of benign (60%), borderline (10%) and malignant (30%) cases with their demographical and histological features. FNAC was the commonest modality of preoperative diagnosis. Table 2

Phyllodes tumors predominantly occur in middle aged women & rarely seen in adolescences and elderly females.<sup>7</sup> They are lobulated masses which may grow rapidly & cause unilateral breast enlargement or even ulceration of overlying skin. They are large in size, more than 10cm but can present 2cm or less in diameter also. Cut surface show a characteristic bulbous protrusions with visible clefts. Large tumors exhibit cystic spaces & foci of hemorrhage. Histologically they are classified into benign, borderline and malignant according to the features of tumor margins, stromal overgrowth, tumor necrosis, cellular atypia and number of mitosis per high power field.[Table 1].

Benign phyllodes tumors resemble clinically and can synchronously occur with fibroadenomas. At least 12.5% of patients have a history of fibroadenoma & 20% of patients have a concurrent diagnosis of benign fibroadenoma. But unlike them tend to recur and may progress to malignant tumors. It was earlier considered as a stromal neoplasm and possibly arises from fibroadenoma. But molecular studies have proved that both component can become neoplastic. The mean age at presentation was 35years. Our patients complaint of painless growing mass of two months to two years duration, commonly found in the right breast. Few can have a huge fungating tumor with ulceration.<sup>8</sup> Two out of six had bilateral tumors, one with a fibroadenoma in contralateral and the other in ipsilateral breast. The largest size was 10cm with grey white areas and cleft like spaces Figure 1A. Multiple section revealed features of benign phyllodes. Figure 1B. The patients were treated by simple mastectomy with or without lymph nodes clearance. However Panda et al.<sup>9</sup> reported in his series of eleven patients secondary changes like haemorrhage, myxoid and cystic degeneration, epithelial hyperplasia, squamous and columnar metaplasia. Unusual features include atypical ductal hyperplasia, DCIS, IDC, synchronous fibroadenoma and tubular adenoma like areas arising within benign phyllodes tumors. We observed extensive sclerosis in the stroma of tumors with longer duration and infarction in one



**Fig. 1:** Benign phyllodes tumor –**A)** Gross specimen A large fleshy grey white tumor with leaf like projections; **B)** Microscopy showing proliferating stroma lined by benign epithelium



**Fig. 2:** Boderline phyllodes tumor **A)**: Gross specimen – A large tumor with bulbous protrusions in cystic spaces; **B)**: Microscopy showing increased stromal cellularity, nuclear atypia and mitosis

**Table 1:** Histopathology criteria for classification of Phyllodes tumor<sup>2,3</sup>

Histopathology features	Benign	Boderline	Malignant
Tumor margins	Pushing margins	Microscopic invasion	Infiltrating margins
Stromal cellularity	Increased	Increased	Increased
Stromal atypia	Mild to moderate	Cellularity & atypia	Atypia
Mitosis/ 10 hpf	<4/10hpf	4- 10/10hpf	10 /hpf

**Table 2:** Demographical distribution and pre-operative diagnosis of ten cases (2012-2017)

S. No	Age /sex	Laterality	Duration	Preoperative Diagnosis FNAC/ Biopsy/ USG
1	50yrs/F	Left	1.5 yrs	FNAC- cellular fibroadenoma
2	45yrs/F	Right	14yrs	FNAC & Biopsy- inconclusive
3	40yrs/F	Left	Not Available	FNAC- Benign phyllodes tumor
4	24yrs/F	Right	2-3yrs	FNAC- cellular fibroadenoma
5	50yrs/F	Right	Not Available	Not Done
6	21yrs/F	Bilateral	1year	FNAC- Fibroadenoma
7	27yrs/F	Bilateral	2-3mths	FNAC- Left- phyllodes tumor Right - Fibroadenoma
8	86yrs/F	Left	1year	Not Done
9	23yrs/F	Not Available	Not Available	Not Done
10	45yrs/F	Right	2years	Not Done

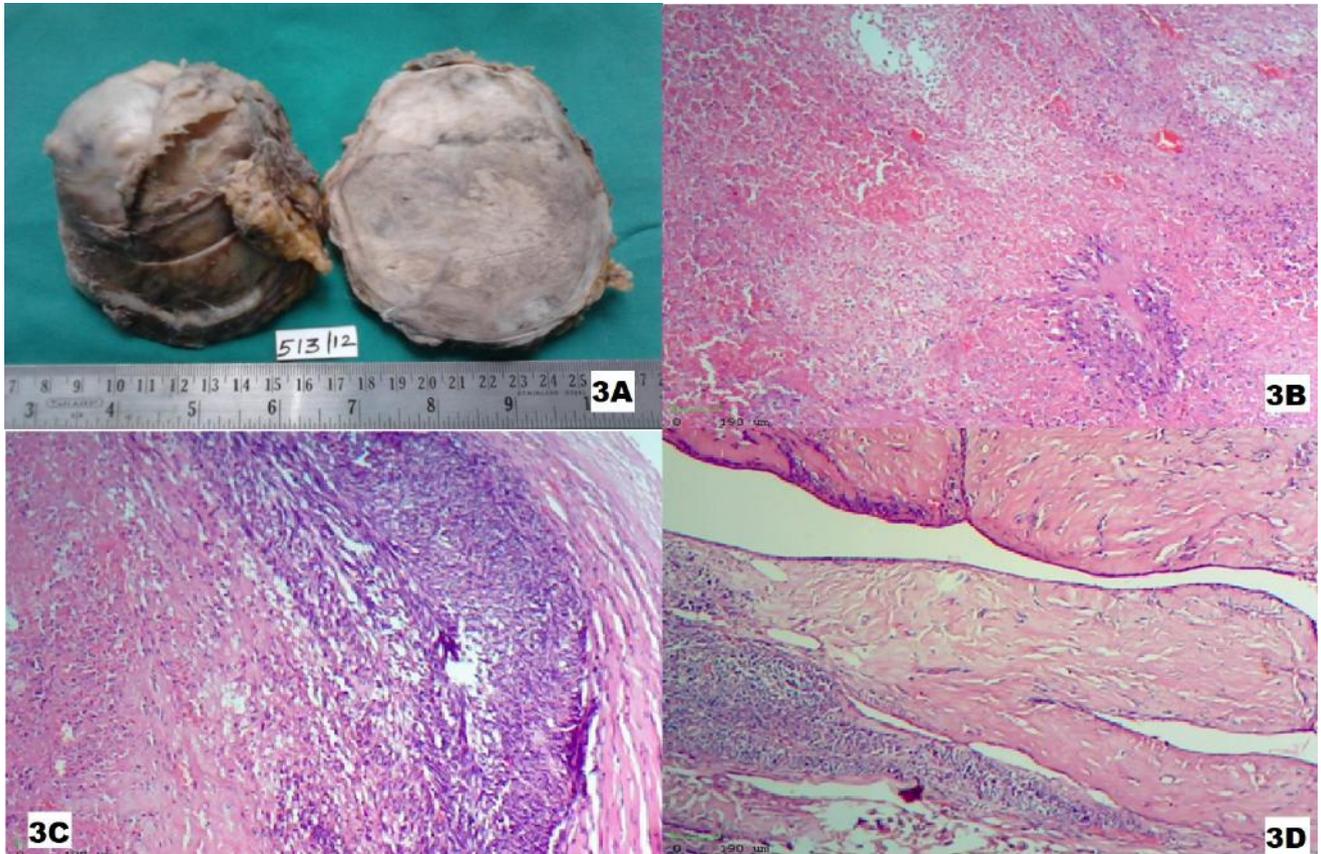
**Table 3:** Tumor size, type of surgery and post -operative histopathology diagnosis

S.No.	Tumor size (maximum)	Surgery Done	Post-operative histopathological Diagnosis
1	8x8cm	Lumpectomy	Benign phyllodes tumor
2	10 x10cm	MRM with axillary lymph nodes	Malignant phyllodes tumor with lymph node metastases
3	17x10cm	Simple Mastectomy	Boderline phyllodes tumor
4	3x2cm	Lumpectomy	Benign phyllodes tumor
5	6x4cm	Lumpectomy	Benign phyllodes tumor
6	8x7cm 6x4cm	Lumpectomy - bilateral	Benign phyllodes tumor Benign phyllodes tumor
7	12x10cm 2x1cm	Simple Mastectomy unilateral synchronous	Benign phyllodes tumor Fibroadenoma
8	15x7cm	Simple Mastectomy with lymph nodes	Malignant phyllodes tumor without lymph node metastases
9	8x4cm	Lumpectomy	Benign phyllodes tumor
10	20x17cm	Simple Mastectomy with lymph nodes	Malignant phyllodes tumor without lymph node metastases

of the contralateral benign phyllodes tumor. This study recommended adequate and extensive sampling for accurate diagnosis.

Borderline malignant tumors are difficult to predict as their biological features have two way differentiation, one with tendency to be benign with good prognosis while other with poor prognosis. Hence histology alone does not guide for treatment and prognosis. Assessment of malignant potential is based on different histologic al features wherein adequate tissue sections play an crucial role. Amel et al.<sup>9</sup> reported a rare case of borderline tumor with simultaneous intraductal and invasive duct carcinoma in a 52 year female. The other subtypes include tubular carcinoma and squamous cell carcinoma. The coexistence of both tumors, as

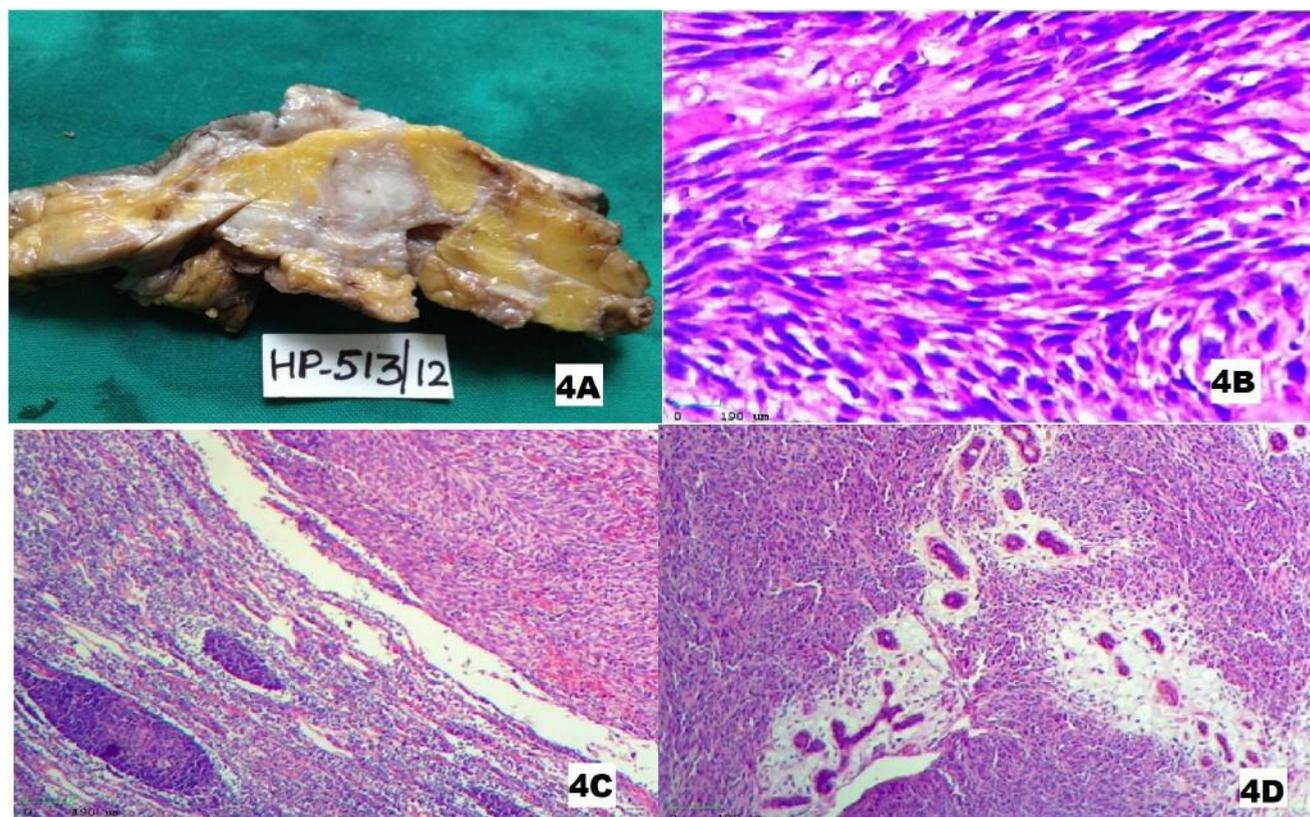
considered by some authors, is due to sudden transformation of the hyperplastic epithelium of the phyllodes tumor or is caused haphazardly in the mammary gland adjunct to phyllodes tumor. In most cases preoperative assessment of existence of a carcinoma and phyllodes tumor is very difficult. We report a case of borderline phyllodes tumor in a 35years female who diagnosed as benign phyllodes tumor on FNAC. H& E sections on extensive sampling showed a foci with increased mitosis 2-3/ hpf and nuclear atypia.[Figure 2B] The patient was treated by simple mastectomy with surgical clear margins. Positive margins after surgery has high local recurrence rate and should be considered for additional local therapy.



**Fig. 3:** Malignant phyllodes tumor **A)**: Gross specimen- A Lobulated mass measuring 10cm in diameter, cut surface shows areas of necrosis with viable tumor at the periphery. **B)**: Microscopy showing – 1) coagulative necrosis 2) leaf like projections lined by benign epithelial cells 3) atypical spindle cells 4) lymph node metastases. (H&E,100X)

Malignant phyllodes tumor are rare as compared to adenocarcinoma of breast.<sup>10</sup> They grow to reach large size and undergo necrosis. A tumor is considered malignant if stromal component show features of sarcoma. Heterologous sarcomatous differentiation is rare and has been reported by Nayak et al.<sup>11</sup> in their series of nine cases in the form of angiosarcoma, fibrosarcoma, undifferentiated sarcoma, extensive squamous differentiation and lipomatous metaplasia. The report also emphasizes the importance of accurate diagnosis and subtyping of the components for correct treatment modalities and to predict the prognosis. However treatment modalities are limited with no clear protocols. Histologically, this malignant tumor should be differentiated from metaplastic carcinoma, primary sarcoma and fibromatosis. However, the stromal elements along leaf like epithelial clefts are characteristic features of phyllodes tumor not seen in the other lesions. Immunohistochemistry is of help to distinguished these tumors. Increased expression of p53 protein and Ki-67 antigen has been detected in malignant tumors, however these can also be used to differentiate fibroadenomas from benign tumors.<sup>1,2</sup>

Generally, 10-40% of these tumor take a malignant course with a high tendency towards local recurrence & systemic dissemination.<sup>12</sup> Approximately, 3-12% metastasis which occur at the time of presentation or late as 12yrs spread hematogenously to lungs, bones, brain & liver. Lymph node metastasis is very rare. Incidence range from 1.1-3.8%, hence axillary dissection is rarely recommended. Only few cases of malignant phyllodes with lymph node metastases have been reported in the literature.<sup>12,13</sup> One of our rare malignant case presented large tumor progressively growing for 14 years with lymph node metastases on recurrence. Sonomamography was suggestive of giant fibroadenoma with enlarged axillary lymph node. FNAC followed by biopsy was inconclusive, so lumpectomy was done. We received a large lobulated mass measuring 10 cm in diameter, cut surface predominantly necrotic with fleshy areas at the periphery.[Figure 3A] Multiple sections taken reveal extensive areas of tumor necrosis with scanty viable tumor at the periphery composed predominantly of high grade sarcoma & focal leaf like projection lined by benign epithelial cells at the edge of the tumor. Tumor was composed of atypical spindle cells with pleomorphic



**Fig. 4:** Recurrence of malignant tumor **A):** Grossspecimen of right MRM Showing satellite nodule adjacent to primary tumormeasuring 3x2cm, grayish white with infiltrating margins. **B):** Microscopy of satellite nodule; **A):** Highgrade sarcoma **B):** Tumor infiltrating into breast parenchyma; **C):** lymph nodemetastasis of stromal component (H&E,400X)

hyperchromatic nuclei with a mitotic rate of 3-4/ hpf. Figure 3B However, multiple sections did not reveal any heterologous element stromal component. So a revised MRM with axillary dissection was done. Cut surface revealed a satellite nodule measuring 3x2 cm adjacent to the primary tumor grey white infiltrating into the surrounding breast parenchyma. [Figure 4A] Two lymph nodes dissected were grossly metastatic. Histopathology revealed same morphology as the primary tumor. Lymph node revealed metastasis of stromal component only. Figure 4B The most important differential diagnosis was sarcomatoid carcinoma. However, IHC was negative for epithelial markers, thus confirming malignant phyllodes tumor. Primary sarcoma should also be thought of if there is lack of epithelial component. Approximately 3-12% of malignant phyllodes tumor spread to lungs 66%, bone 28% & brain 9% and rarely to liver & heart. Regional lymph node enlargement is common but lymph node are rarely involved by tumor. Incidence of axillary lymph node involvement is 1.1-3.8% only few cases of malignant phyllodes with lymph node metastases have been reported in literature Rest two cases did show any lymph node metastases.

Wide local excision with a radial margin of at least 1-2cm margin, is the main stay of the disease treatment & free surgical margins are of crucial importance because recurrences is strongly co-related with inadequate and narrow surgical margins.<sup>14</sup> In large tumors, (more than 10cm) & multiple recurrences, mastectomy may be necessary to provide adequate margin. The local recurrences rate ranges from 10% to 40% has been reported in many studies.<sup>2,15</sup> Exploratory analysis by Rodrigues et al.<sup>16</sup> suggested that infiltrative tumor borders may be used in conjunction with margin status to assess local recurrence risk. Such patients should be treated by local therapy. Axillary lymph node dissection is not routine unless nodes are enlarged. Chemotherapy and hormone therapy has not been established even in high grade tumors.<sup>1,2</sup> Radiotherapy is occasional but rarely used and is only recommended for cases with positive or near positive surgical margins and in selected cases for whom further surgical procedures cannot be performed.<sup>17</sup> Combination of adjuvant chemotherapy and radiotherapy should be considered in malignant tumors as encouraging results are seen in soft tissue sarcomas. In patients with multiple recurrence, the disease is controlled with full thickness chest wall resection which involves

excision of pectoralis muscle, followed by reconstruction of the chest wall with marlex or latissimus dorsi muscular / myocutaneous flap if the fascia or muscle is infiltrated.<sup>2,18</sup>

In one of our malignant case, two months later patient came with recurrence at scar site. Biopsy was reported as high grade sarcoma. CT scan of thorax revealed no evidence of lung or pleural involvement. Patient underwent wide local excision with 5cm tumor free margins and excision of 4th rib. This defect was closed by TRAM flap. Patient recovered and is followed up. The other two malignant tumor cases were treated by simple mastectomy and had no lymph node metastases.

A study conducted by Jia C et al.<sup>19</sup> states the relationship between morphological features grading, diagnosis and prognosis in phyllodes tumor. They conclude that each parameter in the histological grading of phyllodes tumor may have different prognostic value and markedly increased mitotic count were predictive of relapse of the tumor. Of all risk factors, Ganesh et al.<sup>20</sup> found that the presence of tumor necrosis is significantly associated with increased incidence of recurrence, local or distant and is a negative prognostic factor.

Thus a review of available literature on phyllodes tumor suggests that more radical treatment fails to prevent metastases, therefore conservative surgery followed by close follow up of is all that is needed.<sup>21</sup> To define and update new chemotherapeutic drugs for optimal treatment to these patients, multi-institutional trials should be carried out.

## 6. Conclusion

Phyllodes tumors are uncommon tumors of breast occurring in middle age women and should be included in the differential diagnosis of breast lumps. Our study reveals bilateral and synchronous occurrence of phyllodes tumor clinically and a rare case of malignant tumor with lymph node metastases. Histologically, unusual findings were presence of extensive sclerosis and necrosis in borderline and malignant phyllodes tumor respectively. Irrespective of the histological type they are known to recur as the biological behaviour cannot be predicted. Extensive and adequate sampling should be done in large tumors to differentiate it from other primary tumors of the breast. Pre-operative diagnosis and proper management by ensuring clear surgical margins plays a crucial role in preventing recurrence of this tumor.

## 7. Source of funding

None.

## 8. Conflict of interest

None.

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