



Histopathological Spectrum Of Phyllodes Tumor Of Breast In A Tertiary Care Centre

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Abstract

Background: Phyllodes tumors of the breast are rare tumors classified into histological types benign, borderline and malignant. These fibroepithelial tumors may recur and metastasize. Clinical, radiological and histological examination is required for categorisation. Phyllodes show a spectrum of histological features like hyperplasia, metaplasia, dysplasia, in situ and invasive ductal malignancies in epithelial component while stromal component shows heterologous differentiation, needs to be differentiated from primary sarcomas.

Materials And Methods: Retrospective study done for one year duration includes patients presenting with lump in breast, diagnosed as phyllodes tumor on histopathology. Demographic data, clinical status and histopathological findings were retrieved and analysed.

Results: Thirteen cases of phyllodes tumors were diagnosed histologically and categorized into benign(46%), borderline(31%) and malignant(23%). 12 cases were female(92%) and 1 male(8%). Unilateral involvement noted in eleven and bilateral involvement in two cases. Tumor size ranges from 3cm in benign and 17cm in malignant tumors. Three malignant tumors presented with >10 mitotic figures/10 HPF with one having lymph node metastasis. Two cases showed phyllodes in ipsilateral and fibroadenoma in contralateral breast.

Conclusion: Phyllodes tumors are uncommon tumors of breast in middle aged women and are important in differential diagnosis of breast lumps. This study reveals the abnormal distribution of these cases referred to tertiary care center in north western India. Irrespective of the histological type they may recur, extensive and adequate sampling in large tumors helps in differentiation from primary tumors. Pre-operative diagnosis, adequate management and ensuring clear surgical margins allow prevention of tumor recurrence.

Keywords: Phyllodes, fibroepithelial, breast, benign, borderline, malignant

Introduction

Phyllodes tumors are rare biphasic tumors occurring in breast tissue¹. Phyllodes tumour of the prostate is an extremely rare prostatic neoplasm with great variability in the histological appearance and clinical behaviour of this tumour, less than 90 cases were reported to date². Phyllodes tumor shows a spectrum of histological features such as hyperplasia, metaplasia, dysplasia, in situ and invasive ductal malignancies¹ in epithelial and mesenchymal component. They are a group of fibroepithelial

lesions of breast typically presenting as mobile and painless mass in breast.

These tumors were classified into types: benign (60-75%), borderline(15-16%) and malignant (10-30%), according to new WHO classification based on stromal characteristics, these characteristics included the degree of atypical cellular stroma, mitotic activity per 10 high power fields, the presence or absence of stromal overgrowth, tumor necrosis, infiltrative tumor margins or well-defined tumor margins and presence of malignant heterologous stromal elements³.

The incidence is about 0.3–0.5% of all breast tumors and the frequency of malignant lesions varies from about 5% to 30%. These tumors are present at all ages, most commonly seen in the 3rd and fourth decades.

Therefore this study presents a summary of the spectrum of clinical and histological features of 13 cases diagnosed as phyllodes tumors in one year duration in a tertiary care centre.

Material And Methods:

The present study is a retrospective study conducted at Mahatma Gandhi Medical College and Hospital, Jaipur, India over a period of one year from May 2021 to April 2022. In this study 13 patients presenting with lump in breast that underwent either lumpectomy or mastectomy diagnosed as phyllodes tumor are included taking into consideration their demographic data, clinical features and histological diagnosis.

Results:

Out of the 13 cases included, one case is male of 65years diagnosed as poorly differentiated neoplasm, and the rest are females with mean age of presentation of 39years, the youngest is 28years old. All cases presented with painless enlargement of breast mass for few months to two years. Unilateral involvement of breast is mostly seen, with bilateral involvement in two patients. All the thirteen cases of phyllodes tumors were diagnosed histologically by following WHO criteria into benign (46%), borderline (31%) and malignant (23%). Histologically, type of margins, stromal cellularity, atypia and mitosis were assessed. The tumor size ranges from 3cm in benign and 17 cm in malignant tumors in the greatest dimension. Out of the malignant tumors, all three presented with more than 10 mitosis figures per high power field and one presented with lymph node metastasis

Table I: Distribution according to age

Age group	Number of cases	Percentage
26-35yrs	3	23%
36-45yrs	6	46%
46-55yrs	3	23%
56-65yrs	1	8%
Total	13	100%

Table II: Distribution according to gender

Gender	Number of cases	Percentage
Female	12	92%
Male	1	8%
Total	13	100%

Table III: Distribution according to laterality

Laterality	Number of cases	Percentage
Unilateral(Left side)	8	62%
Unilateral(Right side)	3	23%
Bilateral	2	15%
Total	13	100%

Table IV: Distribution according to duration, tumor size and specimen

S.No	Duration	Tumor size	Specimen
1	8months	17x11x9.4cm	Left breast MRM
2	6months	Not known	Right breast mass, core biopsy
3	12months	3x3x2.5cm	Breast lump, wide excision
4	14months	4x4x3cm	Lumpectomy
5	7months	12x10x9.5cm	Right breast lumpectomy
6	8months	14x12x8.8cm	Left breast MRM
7	12months	10x10x9cm	Left breast lumpectomy
8	15months	3.5x2x2cm	Left breast lumpectomy
9	12months	11x8x8cm	Left breast MRM
10	Not known	4x3x3cm	Bilateral breast tissue
11	12months	5.5x4x4cm	Right breast lumpectomy
12	8months	9x8x6.5cm	Left breast MRM
13	5months	9.5x8.5x7cm	Left breast MRM

Table V: Distribution according to histological type

Histological Type	Number of cases	Percentage
Benign	6	46%
Borderline	4	31%
Malignant	3	23%
Total	13	100%

Table VI: Distribution according to Histological characteristics

S.No	Histopathological type	Stromal Cellularity	Stromal Atypia	Stromal overgrowth	Mitotic activity	Tumor border	Lymph node status
1	Borderline Phyllodes tumor	Moderate	Mild to moderate	At places	5-6/10HPF	Focally Infiltrating	0/10 Lymph nodes show reactive hyperplasia
2	Benign phyllode tumor	Not known	Not known	Not known	None	Not known	Not known
3	Benign phyllodes tumor	Mild	None	Absent	None	Circumscribed	Not known
4	Borderline Phyllodes tumor	Moderate	Moderate	At places	4-5/10HPF	Focally Infiltrating	Not known
5	Benign phyllodes tumor	Mild	Mild	Absent	1-2/10HPF	Circumscribed	Not known
6	Borderline Phyllodes tumor	Moderate	Mild to moderate	Absent	4-5/10HPF	Focally Infiltrating	Not known
7	Borderline Phyllodes tumor	Moderate	Mild to moderate	At places	5-6/10HPF	Focally Infiltrating	Not known
8	Benign phyllodes tumor	Mild	None	None	None	Circumscribed	Not known
9	Malignant phyllodes tumor	Marked	Marked	Present	>10/10HPF	Focally Infiltrating	2/22 show metastatic tumor deposits
10	Benign phyllodes tumor	Mild	Mild	Absent	1-2/10HPF	Circumscribed	Not known
11	High grade sarcoma	Marked	Marked	Present	12-15/10HPF	Focally Infiltrating	Not known
12	Poorly differentiated malignant neoplasm	Marked	Moderate	Present	11-12/10HPF	Focally Infiltrating	0/10 Lymph nodes show reactive hyperplasia
13	Benign phyllodes tumor	Mild	Mild	Absent	1-2/10HPF	Circumscribed	Not known

*HPF – High power field

Figure 1: A) Benign Phyllodes Tumor : A large, fleshy grey white tumor with leaf like projections B) C) H&E Benign phyllodes 100x, D) H&E Benign phyllodes 400x

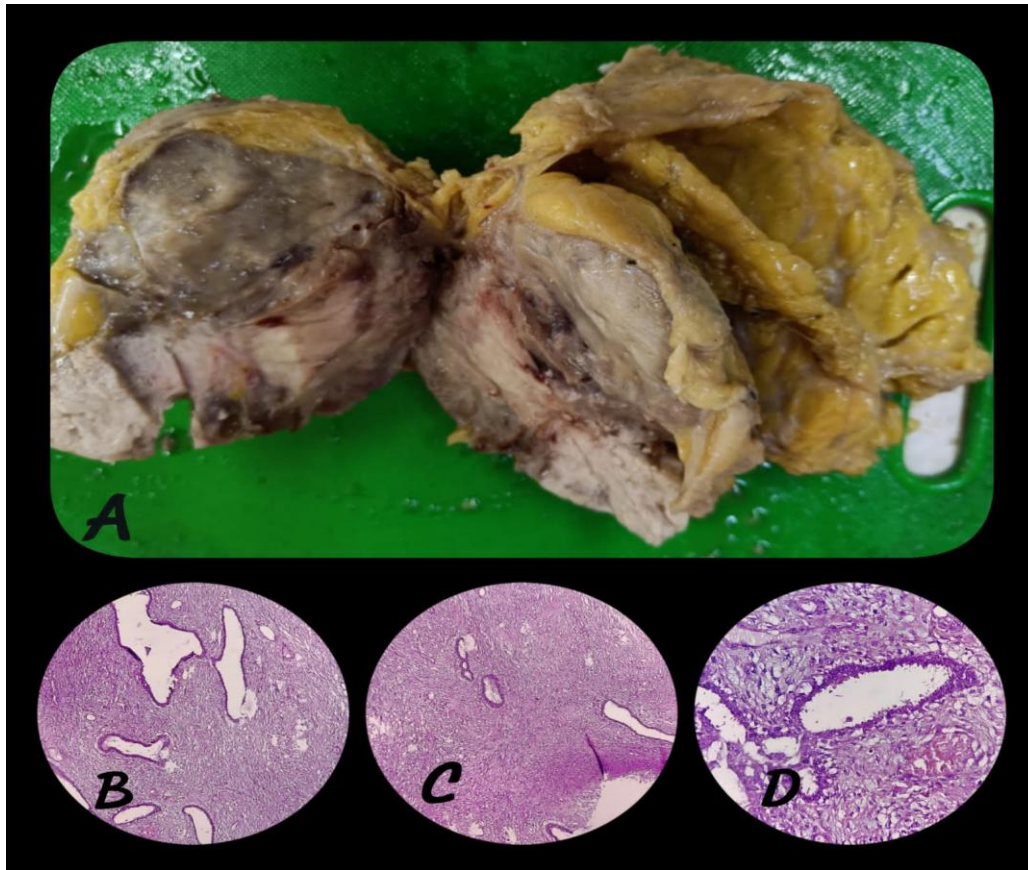


Figure 2 : A) B) H&E Borderline phyllodes tumor 100x, C) H&E Borderline phyllodes tumor 400x

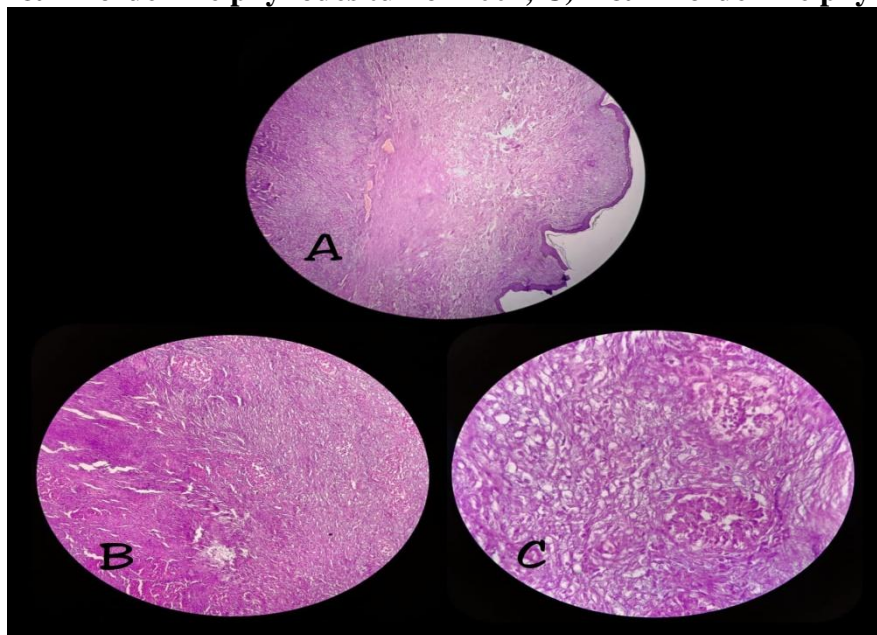
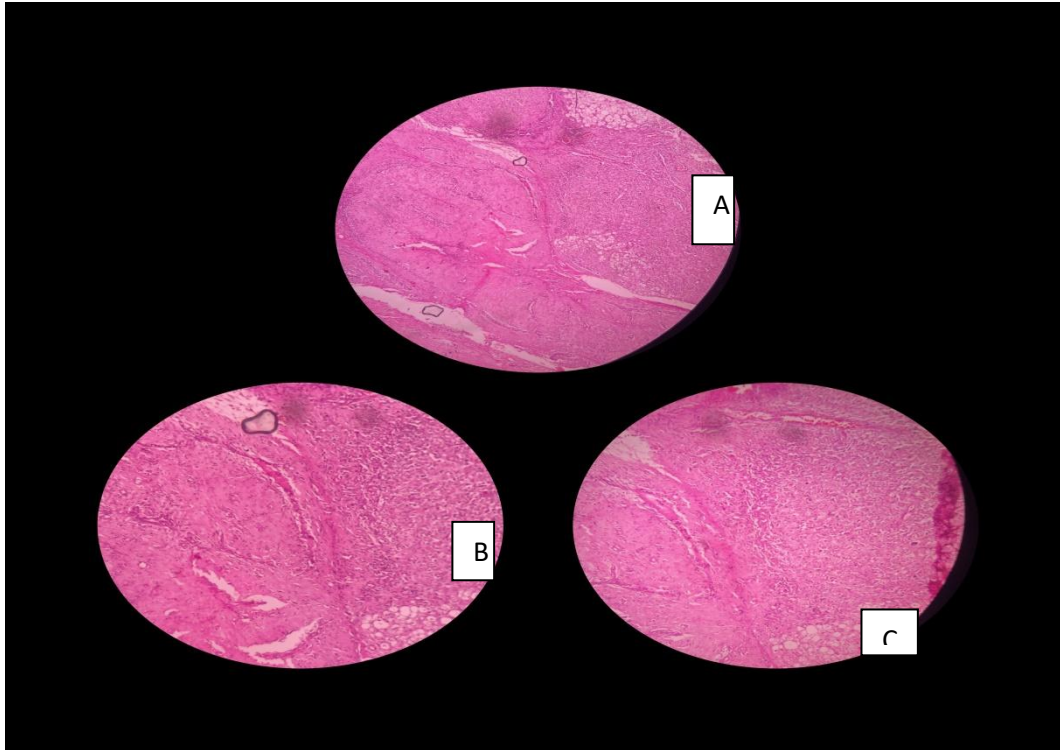


Figure 3 : A)B)C) H&E Malignant phyllodes tumor**Discussion:**

Phyllodes tumors are rare lesions, occurring 0.4–1% of all breast tumors¹. 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 behavior of this tumor¹. Phyllodes tumor of the breast is rare and mainly observed in middle-aged women, with a widely varying mean age of from 30 to 52 years.

It was then adopted by WHO as phyllodes tumor and based on histomorphological criteria, Rosen subclassified them into benign, borderline & malignant tumors. The biphasic pattern, namely the epithelial and stromal component differentiates it from other primary tumor like sarcomas. Mostly these tumors are benign (35% to 64%), rest are borderline and malignant sub types. Clinical, radiological and histological examination forms the fundamental basis for the evaluation of phyllodes tumors. These tumors have a wide spectrum of clinical and morphological features they may cause difficulties in pre-operative diagnosis³.

All the thirteen cases of phyllodes tumors in this study are diagnosed histologically by following WHO criteria into benign (46%), borderline (31%) and malignant (23%) cases with their demographical and histological features. Sawant SA et al (2020) showed that out of ten cases of phyllodes tumor 60% were benign, 10% were borderline and 30% were malignant (30%).

Phyllodes tumor are lobulated masses which may grow rapidly & cause unilateral breast enlargement or ulceration of overlying skin. They may be large in size, more than 10cm or can present 2cm or less in diameter also. Cut surface shows characteristic bulbous protrusions with visible clefts. Large tumors exhibit cystic spaces & foci of hemorrhage. They are classified histologically into benign, borderline and malignant according to the features of tumor margins, stromal overgrowth, tumor necrosis, cellular atypia, malignant heterologous stromal elements and number of mitotic figures per 10 high power field.

Benign phyllodes tumors have mild stromal hypercellularity, minimal to no stromal atypia, no stromal overgrowth, circumscribed (pushing) tumor borders and less than or equal to 4 mitoses per 10 high-power fields (HPFs). Phyllodes tumors are

classified as malignant when all five of the following histological features are present: marked stromal hypercellularity; marked stromal atypia; stromal overgrowth; an infiltrative (permeative) tumor border; and greater than or equal to 10 mitotic figures in 10 high power fields. Tumors should be classified as borderline if some but not all of these changes are present.

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. In the present study two out of thirteen cases (15%) showed concurrent fibroadenoma in contralateral breast.

Panda et al.(2016) reported in his series of eleven patients diagnosed as phyllodes tumor, 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 tumors⁵.

Borderline malignant tumors pose a difficulty as their biological features can show differentiation, one with tendency to be benign with good prognosis while other with poor prognosis so histology alone does not guide for treatment and prognosis. Assessment of malignant potential is based on different histological features requiring adequate tissue sampling. Amel et al. (2010) reported a rare case of borderline tumor with simultaneous intraductal and invasive duct carcinoma in a 52 year female. In their study five cases were reported as borderline phyllodes tumor in age group 30-45 years age and tumor size ranging from 4-17cm in greatest dimension.

Malignant phyllodes tumor are rare tumors accounting for $\leq 1\%$ of all primary breast neoplasms. They may reach large sizes 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.⁶ (2017) including angiosarcoma, fibrosarcoma, undifferentiated sarcoma, extensive squamous differentiation and lipomatous metaplasia. As per WHO guidelines well differentiated liposarcoma is not included in heterologous differentiation. The

report also targeted the need for 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, malignant phyllodes tumor should be differentiated from metaplastic carcinoma, primary sarcoma and fibromatosis. 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 literature⁶. Present study also showed one case of malignant phyllodes tumor with lymph node metastasis.

The American Joint Committee on Cancer (AJCC) eighth edition and the World Health Organization (WHO) recommended staging malignant phyllodes tumors on the basis of size of tumor and lymph node involvement, and presence of malignant heterologous mesenchymal component (e.g. liposarcoma, chondrosarcoma, osteosarcoma) even if the other histological parameters are not present, or if only some are present. T category, N category and stage group assignments do not apply to benign or borderline phyllodes tumors and should only be reported if the tumor is malignant. Further confirmation required by IHC includes pancytokeratin, vimentin, epithelial membrane antigen, smooth muscle actin, desmin, myogenin, S-100, P63, CD31, CD34, BCL-2 and CD117 wherever indicated.

Conclusion:

Phyllodes tumors are uncommon tumors of breast, mostly observed in middle aged women and are one of the important differential diagnosis of breast lumps. Irrespective of the histological type they are known to recur. 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 prevents the recurrence of this tumor

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