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# Histomorphological spectrum of Phyllodes Tumours: A Restrospective Study

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## ABSTRACT

**Introduction**: Phyllodes tumours are rare fibroepithelial lesions of breast. Clinical examination, ultrasound, cytology and histopathology are the mainstay of the diagnosis. The present research was undertaken with the aim of studying the clinicopathological features of Phyllodes tumour reported in the past seven years in a Delhi government hospital.

**Method:** A retrospective study of phyllodes tumour was carried out in females from 225 diagnosed cases of breast lesion reported in the pathology department of a government hospital in Delhi during the period of January 2013 to December2019. All the relevant history, findings of clinical examination and investigations performed were assessed from files of the patient.

**Results**: Out of 225 cases of breast lesions reported in the pathology department 8 tumours were reported as phyllodes in the study period. The most common affected age group was 41- 50yrs. 5 (62.5 %) of 8 tumours were benign,2 (25) %) were borderline and only 1 was malignant. The tumour size was 15mm to 200mm. All the 8 cases (100%) presented with breast lump; 3 cases (30%) complained of pain in the lump. 2 cases developed ulceration and Peau D' orange and in 1 case typical nipple retraction was seen. FNAC was done in 5 patients. No preoperative investigations were done in 2cases.

**Conclusion**: Phyllodes tumour is a rare neoplasm of the breast. Histopathology plays an important role in differentiating it from fibroadenoma. Strict histologic assessment is definitely required for the diagnosis of the PT and for its treatment and management

**KEYWORDS:** Phyllodes Tumour, Fibroeithelial Lesions, Fibroadenoma

## INTRODUCTION

Phyllodes tumours (PT) of the breast are rare biphasic tumours that exhibit proliferation of both epithelial and stromal components. They account for less than 1% of all primary breast tumours with risks of local recurrence and distant metastases.[1]Johannes Muller in 1838 named these tumours as"cystosarcomaphyllodes" due to leaf like projections of the stroma into the cystic spaces.[2]However, in 1982 WHO adopted the term "phyllodes tumour" for their nomenclature.[3]Based on histopathological features such as stromal cellularity, stromal cell atypia, stromal overgrowth, mitotic activity, tumour margins and the presence of malignant heterologous elements WHO has classified these tumours into benign, borderline and malignant.[4]Recently, WHO has removed well-differentiated liposarcoma as a criterion of malignancy in breast phyllodes tumours in the absence of other supporting histological features [3].PT presents as a morphologic spectrum from benign to malignant tumours. Differentiating fibroadenomas from PT is particularly important because of the difference in their treatment and management. Moreover, the same tumour may have foci of benign, borderline and malignant elements making the gross and microscopic examination of excised tissue extremely important [4] The biology and molecular landscape of Phyllodes is unknown; the most favoured theory being the epithelial- stromal interactions.Genomic sequencing has identified MDM12 somatic mutations in both fibroadenomas and PT, suggesting their common origin. [5, 6] Thus, in absence of clear cut-offs on histology, lack of established biomarkers and unknown molecular biological features of these tumours, diagnosis of PT remains a challenge. The present study was undertaken to analyse the clinicopathological features of phyllodes tumour of the breast in a government hospital in Delhi.

**MATERIALS AND METHODS:**

The present study was a retrospective study of phyllodes tumour in females from 225 cases of breast lesion reported in the pathology department of a government hospital in Delhi during the period of January 2013 to December2019. Patient details including clinical history, examination findings, investigations and final histopathology reports were assessed from patients' files. The cases included for the study were all histologically proven cases of phyllodes tumour who underwent surgery during the period of the study. The exclusion criteria were malignant tumours of the breast other than malignant phyllodes and other benign breast disease.

**RESULT**

In this retrospective study , out of 225 cases of breast lesions reported in the pathology department 8 tumours were reported as phyllodes in the study period.41 to 50 yrs was the commonest affected group with 4 (50%) cases of PT. Lump was seen in all the cases. Pain associated with lump was reported in three cases. Two cases had ulcerated lesion and Peau d" orange and a single case of retracted nipple was seen.Table 2 Cytologically both the stromal and epithelial components and background cells were studied. FNAC were done in 5 patients of which 3 cases were reported as fibroepithelial lesion with differential diagnosis of fibroadenoma and phyllodesFigure 1 and 2 cases were given a diagnosis of fibroadenoma. One case had a FNAC report of fibroepithelial lesion from a different institute. No prior preoperative investigations were available in 2 cases.Table 3

Based on WHO histopathological grading, 5(62.5%)cases of the resected tumours of this study had benign features, [Fig 1] 2 (25%) cases had borderline features and 1 case showed malignant features. Table 4Figure 2 The histopathological correlation with FNAC was done.Table 3

| Histopathology Report | Frequency [ %] |
|---|---|
| Benign | 5 cases (62.5) |
| Borderline | 2 cases (25) |
| Malignant | 1 cases (12.5) |

**Table 4: Final Histopathology Examination Reports of Samples: n=08**

**DISCUSSION:**

Phyllodes tumours account for 0.3% to 0.5% of female breast tumours and 2.5% of all fibroepithelial breast tumours. [7]Phyllodes commonly affects women in 35 to 55 years age group. The tumour is rarely found in adolescents and the elderly. [8]In our study the age group most commonly affected was 40 to 50 years.

Phyllodes display a fascinating spectrum of clinicopathological features ranging from purely benign to dangerously malignant tumours with high potential of rapid growth and metastasis. On the other hand, there are benign PT which are indistinguishable from fibroadenomas. In the malignant PT, epithelial interaction is thought to be the pathogenesis of the malignant transformation of PT. [9]Painless breast lump is the most common presentation of Phyllodes tumour, seen in 76 % cases. Predominantly they are unilateral (96%) however bilateral PT has also been reported. [10] Our results are comparable to above study.

Phyllodes tumours present as fast-growing mass but are clinically benign. Mastalgia is also seen in few cases. Malignant tumours are larger and rapidly growinghowever, size and growth rate are poor predictors of the final histopathological type. [11]

On clinical examination the mass in some shows bosselation, skin shows dilated veins. The lesion can also be ulcerated leading to bleeding, infections and foul-smelling discharge. Retraction of nipple is an uncommon finding. [11]Enlarged axillary lymph nodes have been reported in 10% to 15% cases. The lymphadenopathy seen in PT is more often reactive hyperplasia because of tumour necrosis or ulcerated lesion [10].

No mammographic and ultrasound indicators have been identified that allows differentiation between benign and malignant tumours. [12]Hence the phyllodes tumour can be extremely difficult to differentiate from a fibroadenoma. Thus, the need for early and correct diagnosis cannot be overemphasized. Management of such cases which is often surgical intervention can then be performed at the earliest. Chua et al. studied 106 patients and found that 71% of the patients who turned out to be PT were presumptive diagnosed as FA. [13]Thus the correct cytological diagnosis of PT is fraught with difficulties as both phyllodes tumour and fibroadenoma are fibroepithelial lesions. There are many prior studies which have proven that FNAC is not promising, Salvadori et al. found the FNA to be diagnostic in only 4 of 30 case. [14]Review of literature shows a diagnostic accuracy of FNAC to be only 63% which emphasizes the need of histopathology for final diagnosis. [15] In our study also there was difficulty in differentiating fibroadenoma from phyllodes on FNAC thus a differential diagnosis of fibroepithelial lesion was given. The smears showed variable regions of hypercellular stroma in two cases and thus made it difficult in distinguishing fibroadenomas with cellular stroma from low-grade phyllodes tumours . Thus, diagnosis of fibroepithelial lesion was given with a differential diagnosis of Phyllodes tumours and fibroadenoma. It was confirmed as benign phyllodes later on histopathology. In another case as the smear were hypercellular showed enlarged and atypical stromal nuclei thus the differential diagnosis of a fibroadenoma and low grade phyllodes tumour, was given & later it was confirmed as borderline phyllodes on histopathology. Other investigators also have obtained similar results and have concluded that FNA is usually non-

| | Margin | Stromal atypia | Mitosis /10HPF | Stromal overgrowth |
|---|---|---|---|---|
| Benign | Pushing | Minimal | <5 | Absent |
| Borderline | Pushing / infiltrating | Moderate | <10 | present |
| Malignant | Infiltrating | Severe | >/=10 | present |

**Table 1: Three-Tiered Grading System for Phyllodes Tumours Based on 2012 World Health Organization Classification**

| **Presentations** | **Frequency (f)** | | |
|---|---|---|---|
| **Lump** | **Right breast 05** | **Left breast 03** | **Bilateral 0** |
| **Pain** | **03** | | |
| **Nipple retraction** | **01** | | |
| **Skin changes** | **02** | | |
| **Bosselated surface** | **01** | | |

**Table 2: Mode of presentations of phyllodes tumour n=08 [ No of cases]**

| Preoperative investigation | No. of cases frequency(f) | Report given on FNAC | Histopathology report |
|---|---|---|---|
| FNAC | 5 cases | **3 cases as fibroepithelial lesion with D//d of fibroadenoma phyllodes 2 cases fibroadenoma** | **1 case as borderline phyllodes2 cases as benign phyllodes 2 benign phyllodes** |
| Outside report (FNAC) | 1case | **Fibroepithelial lesion** | **Benign phyllodes tumour** |
| No prior investigation was available | 2 cases | | **1 malignant phyllodes tumour 1 borderline phyllodes tumour** |

**Table 3: Preoperative (FNAC) investigation done on phyllodes tumour and its comparison with histopathology**

Fig 1

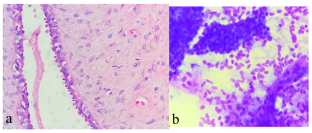


**Figure 1: Benign Phyllodes showing leaf like pattern and mild cellular stroma(40X, H&E)Fig (b): FNAC showing cellular stromal component. (40x, Giemsa)**

Fig : 2

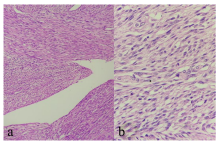


**Figure 2: Malignant phyllodes showing stromal overgrowth, and marked cytologic atypia (10X H&E)Fig (d): Malignant phyllodes with brisk mitotic activity of the stromal component (40X, H&E)**

diagnostic. [16]

A useful alternative to FNAC is core tissue biopsy and many authors have recommended it as a diagnostic tool [13]A sensitivity of 99% with negative predictive value and positive predictive value 93% and 83%respectively has been reported by Komenaka et al. [17]However, in our institute excision biopsy was performed.Phyllodes tumours vary greatly in size from 5 mm to 250 mm, with a mean size of 83mm. [8] Macroscopically, benign small phyllodes tumours showed well circumscribed, lobulated and solid mass with firm consistency. They are tan white to grey and have a whorled appearance on cut surface, similar to a fibroadenoma. But unlike phyllode's, fibroadenomas have a true capsule. The large tumours often show areas of haemorrhagic and necrotic, occasionally fibro gelatinous areas. The tumours are soft and fleshy. [11]On histopathology phyllodes tumour are characterized by stromal overgrowth pattern with intracanalicular growth pattern pushing the epithelium to the periphery forming a leaf like contour. Both epithelial and stromal elements are mandatory for the diagnosis of phyllodes. [10]As compared to fibroadenoma, the stroma of PT is more cellular. The stromal cells of PT are plump spindle-shaped cells, which show pleomorphism. The stroma is the neoplastic element of the tumour and it determines the pathological behaviour.

On histopathology malignant phyllodes tumours showed high stromal cellularity, marked cellular pleomorphism, > 10Mf/10HPF, infiltrative margin and stromal overgrowth. The occasional ducts seen in cellular stroma represent the epithelial component. Azzopardi [18] and Salvadori [14]had included borderline category in classification of phyllodes tumour. World Health Organization added stromal atypia (mild, moderate or marked) and a malignant heterologous element in the criteria for diagnosis [4].Histopathological diagnosis of benign and malignant phyllodes tumours is relatively easy, the diagnosis of borderline phyllodes tumors is challenging for the pathologist. Presence of all the histopathological features are not mandatory for a diagnosis of borderline phyllodes tumour. In one of the cases in the present study, the focal permeative nature of the tumor was seen thus the diagnosis of borderline Phyllodes was given. The grading of phyllodes tumour on histological parameters is a subjective phenomenon and does not show a good correlation with their biological behaviour [19]

Haematogenous route is the most common route of metastasis [10]in malignant PTs. The most favoured site is lungs and bones. Metastasis to lymph node is less common

Many immunohistochemistry markers have been studied for their diagnostic role. Few of them are p16, p53, Ki67, EGFR, CD117 and VEGF. [10] The search for adjunct biomarkers that can predict the biological behavior of PT is continuing.MIB-1, S phase fraction, CD34, micro vessel density and factor XII stromal positivity are few of them [20]. Research on over expression of c-myc and c-kit for diagnosis of malignant PT may prove to be beneficial. [20]

The treatment of choice for benign phyllodes is lumpectomy, however large malignant tumours require mastectomy without axillary dissection. Radiotherapy and chemotherapy have also been tried but haven't yet met with expected outcome.

## CONCLUSION

Phyllodes tumour display a wide spectrum of histomorphological features. There is no clear-cut demarcation between PT and FA. Intensive assessment of the various histological features as per WHO classification can help to arrive at the correct diagnosis. The limitation of our study was that core tissue biopsy was not done in our institute and preoperative investigation findings like FNAC was not available in few cases.

Future research in genomic sequencing will certainly help in bringing a paradigm shift from histopathological diagnosis to molecular diagnosis of PT. However, in a low resource setting histopathology will always play a pivotal role in their diagnosis.

## REFERENCES

1. Rosen PP, Oberman HA. Tumors of the Mammary Gland, Atlas of Tumor Pathology. AFIP Third Series. 1993;7.

2. Fiks A. Cystosarcomaphyllodes of the mammary gland–Müller's tumour. For the 180th birthday of Johannes Müller. Virchows Arch APathol Anat Histol. 1981;392(1):1–6.

3. Tan IPH, Ellis K, Allison E, Brogi, Stephen B, Fox S et al.. The 2019 World Health Organization classification of tumours of the breast ; 2020,. doi:doi.org/10.1111/his.14091.

4. Zhang Y, Kleer CG. Phyllodes Tumour of the Breast: Histopathologic Features, Differential Diagnosis, and Molecular/Genetic Updates. Arch Pathol Lab Med. 2016;140(7):665–71.

5. Yoshida M, Sekine S, Ogawa R. Frequent MED12 mutations in phyllodes tumours of the breast. Br J Cancer. 2015;112(10):1703–1708.

6. Piscuoglio S, Murray M, Fusco N. MED12 somatic mutations in fibroadenomas and phyllodes tumours of the breast. Histopathology. 2015;67(5):719–729.

7. Tavassoli F, P. Tumours of the breast and female genital tract. In: and others, editor. Pathology and genetics. vol. 4. Lyon: IARC Press ; 2003,. .

8. Briggs RM, Walters M, Rosenthal D. Cystosarcoma-phylloides in adolescent female patients. Am J Surg. 1983;146:712–726.

9. Karim RZ, Scolyer RA, Tse GM, Tan PH, Putti TC, Lee CS. Pathogenic mechanisms in the initiation and progression of mammary phyllodes tumours. Pathology. 2009;41:105–122.

10. Hayati F, Lian HH, Azizan N, Ali AA, Abidin Z, Suhaili MA. Approaches to phyllodes tumour of the breast: a review article. IntSurg J. 2017;4:841–846.

11. Parker SJ, Harries SA. Phyllodes tumours. Postgrad Med J. 2001;77(909):1760996–1760996.

12. Buchberger W, Strasser K, Heim K, Müller E, Schröcksnadel H. Phylloidestumor: findings on mammography, sonography, and aspiration cytology in 10 cases. AJR Am J Roentgenol. 1991;157(4):715–724.

13. Chua CL, Thomas A, Ng BK. Cystosarcomaphyllodes: a review of surgical options. Surgery. 1989;105:141–188.

14. Salvadori B, Cusumano F, Bo D, Delledonne R, Grassi V, Rovini M et al. ; 1989,.

15. Chhieng C, Cangiarella JF, Waisman J. Fine-needle aspiration cytology of spindle cell lesions of the breast. Cancer. 1999;87:359–371.

16. Mangi AA, Smith BL, Gadd MS, Tanabe KK, Ott MJ, Souba WW. Surgical management of phyllodestumors. Arch Surg. 1999;134:487–93.

17. Komenaka IK, El-Tamer M, Pile-Spellman E, Hibshoosh H. Core needle biopsy as a diagnostic tool to differentiate phyllodestumor from fibroadenoma. Arch Surg. 2003;138(9):12963656–12963656.

18. Benningron JG, Azzopardi J. Sarcoma in the breast. In: J B, editor. Problems in breast pathology. vol. 2. Philadelphia: WB Saunders ; 1979,. p. 355–359.

19. Tan PH, Jayabaskar T, Chuah KL, Lee HY, Tan Y, Hilmy M et al. Phyllodes tumors of the breast: the role of pathologic parameters. Am J Clin Pathol. 2005;123(4):529–569.

20. Yonemori K, Hasegawa T, Shimizu C, Shibata T, Matsumoto K, Kouno T et al. Correlation of p53 and MIB-1 expression with both the systemic recurrence and survival in cases of phyllodes tumors of the breast. Pathol Res Pract. 2006;202(10):705–712.

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