

Phyllodes Tumors of Breast: A Review of 30 Cases

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ABSTRACT

- Objective* To describe clinical features, histopathology, treatment and prognosis of phyllodes tumor of breast.
- Study design* Descriptive case series.
- Place & Duration of study* Department of Surgery, Jinnah Postgraduate Medical Centre Karachi, from 2005 to 2011.
- Methodology* This is a retrospective review of the medical records of patients managed over a period of six years. The data of patients with phyllodes tumor (PT) of breast were analyzed for age at the time of diagnosis, the duration of the illness, tumor size, tumor localization, ultrasound features, preoperative diagnosis, surgical procedure, pathological grading and outcome. Grading of tumor was done according to the World Health Organization (WHO) classification.
- Results* The age of the patients ranged from 19 year to 66 year (mean age 40 year). The mean age of occurrence of benign, borderline and malignant tumors was 35.5, 44.5 and 45.6 year respectively. The mean time from onset of symptoms and pathological diagnosis of PT ranged from one to 36 months (mean 15 months). Tumors occurred in the left breast in 12 cases, and on right side in 16 cases. The upper outer quadrant was involved in 11 (36.6%) cases.
- The resection margin was recorded as negative in 18 cases. Nine patients underwent post-operative radiation (3 borderline and 6 malignant PTs). Local recurrence occurred in one benign, 3 borderline and 2 malignant cases. Treatment in the case of recurrent benign PT included lumpectomy. Mastectomy was done in 5 other recurrent cases.
- Conclusions* Phyllodes tumors of the breast have an unpredictable outcome. A wide local excision, with adequate margin of normal breast tissue, is the preferred initial therapy
- Key words* Phyllodes tumor, Breast tumor, Treatment-breast tumor.

INTRODUCTION:

Phyllodes tumor is a rare fibroepithelial breast neoplasm with unpredictable clinical course that resembles fibroadenoma. It accounts for 0.3% to 1% of all primary breast tumors and 2.5% of fibroepithelial breast lesions.^{1,2} This tumor has a variable but usually benign course, and has a propensity to locally recur and the ability to metastasize.

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PTs commonly found in women between 35-55 year of age. These are classified as benign, borderline and malignant based on cellular atypia, mitotic activity and stromal overgrowth, according to the WHO-classification.¹ The standard treatment for the PT is wide surgical excision with clear margin of more than one cm.³ Most of the phyllodes tumor are not diagnosed pre-operatively. The objective of this study was to describe the clinical diagnosis, histopathological grading, treatment offered and outcome of phyllodes tumor.

METHODOLOGY:

In this descriptive case series study we retrospectively

reviewed the medical records of the patients diagnosed with phyllodes tumor of the breast at Ward-26, Jinnah Postgraduate Medical Centre Karachi from 2005 to 2011. The extracted data included age at the time of diagnosis, the duration of the mass, size of the tumor, tumor localization, ultrasound findings, preoperative diagnosis, surgical procedure performed, pathological grading and outcome. Grading into benign, borderline and malignant was performed on hematoxylin and eosin stained sections, using the World Health Organization classification taking into account stromal cellularity and overgrowth, cellular atypia, mitotic activity and microscopic tumor borders.

The data were entered and analyzed in SPSS version 17. Descriptive statistics was used to summarize the continuous variables and presented as mean \pm standard deviation and categorical variables in frequencies and percentages.

RESULTS:

The age of the patients ranged from 19 to 66 year. The average of patients with benign, borderline and malignant tumors was 35.5, 44.5 and 45.6 year respectively. There were 19 married women, 17 of whom had children. Fourteen were lactating mothers. Five women already had menopause at the time of diagnosis. Eight patients had concurrent fibroadenoma of the same breast while four patients had a family history of breast cancer. Only one patient was pregnant at the time of diagnosis.

All the patients presented with a palpable breast lump. Pain was present in 15 cases and cutaneous signs (skin fixation, nipple retraction, ulceration of the overlying skin) were found in six cases. The mean time from onset of the symptoms and pathological diagnosis of PT ranged from one to 36 months (mean - 15 months). The tumors found in the left breast in 12 cases, in the right breast in 16 cases while in two cases both breast were involved. The upper outer quadrant was involved in eleven (36.6%) cases.

Ultrasound showed a heterogeneous, hypo-echoic, well delineated, and cystic mass suggestive of a PT in six cases. In 16 cases, the diagnosis of fibroadenoma was suggested whereas in eight cases both were reported as differential diagnosis. Fine needle aspiration cytology was performed in all the cases but diagnosis of PT was made in six cases. Surgical treatment consisted of wide local excision in six cases, lumpectomy in 20 cases and total mastectomy in four cases (3 malignant PTs and 1 borderline PT). On gross appearance tumors ranged

in size from 1.5 to 40 cm (mean 7.8 cm). Fourteen tumors were larger than 5 cm. On histological examination 15 tumors were graded as benign, eight as borderline and seven as malignant.

Nine patients underwent post-operative radiation (three borderline and six malignant PTs). Seven patients were lost to follow-up after surgery. Follow-up period of the remaining 21 patients ranged from 5 to 33 months with a mean of 12 months. Six patients experienced local recurrence at the same site in an average period of nine months. Local recurrence was found in one benign, three borderline and two malignant cases. Treatment in the case of recurrent benign PT included lumpectomy and mastectomy in the five other recurrent cases, combined with post-operative chemotherapy in two cases, with both chemo- and radiotherapy in two cases, and with only post-operative radiotherapy in one case (table I).

Lung metastases occurred in 3 patients, one of whom already had local recurrence. Metastatic tumors developed in an average period of 24 months (two years) and were treated by radio- and chemotherapy. Three patients died during the follow-up period because of advanced metastatic disease in one case and from chemotherapy complications in two cases.

DISCUSSION:

Phyllodes tumors are rare and locally advanced neoplasm of the breast. The median age group in which these tumors occur is about 15 years older than the age group for fibroadenomas.⁴ PTs often present as palpable masses, most commonly located in the upper outer quadrant of the breast. In the series of Barrio et al, including 293 cases, 3.4% of the patients had bilateral PT.⁵ In our series, two bilateral PT were seen. PTs usually grow slowly and are often painless. Nipple retraction and bloody nipple discharge may occur when the tumor involves the areolar region.^{6,7} PTs vary greatly in size with a mean size of 4 - 5 cms.

Mammography and ultrasound appearances are nonspecific and the pre-operative diagnosis of PT is difficult. A diagnosis of PT should be considered if sonography reveals fluid-filled, elongated spaces or clefts in a solid mass. It is often difficult to differentiate PT from fibroadenoma. PTs can occur synchronously with fibroadenoma with an incidence higher than seen in the general population.⁵ The percentage of concurrent fibroadenomas varies from 4.2% to nearly one third of women with PTs.^{8,9} In our study the frequency was 26.6%. Histologically,

Table I: Variables Related to Phyllodes Tumor

Characteristics	Benign	Borderline	Malignant
No. of Patients	15	08	07
Age (mean, range)	35.5 (18-55 year)	44.5 (32-52 year)	45.6 (28-62 year)
Size of Tumor (cm)			
Ø = 5 cm	08	03	05
Ø > 5 cm	06	05	03
Surgical Approach			
Ø Breast conserving surgeries	15	07	04
Ø Mastectomy	00	01	03
Histopathological diagnosis	15	08	07
Surgical Margins			
Ø Negative (> 1cm margin)	10	03	05
Ø Close (within 1cm margin)	03	03	04
Ø Inadequate (< 1cm margin)	01	00	01
Outcome			
Ø Recurrence	01	02	03
Ø Metastasis	00	01	02
Patients lost in follow-up	02	03	02

PTs of the breast are biphasic fibroepithelial tumors. The mesenchymal component shows morphologic patterns that range from fibroadenoma-like to frankly sarcomatous tumor.

In a study conducted by Karim et al,¹⁰ benign, borderline and malignant PTs ranged between 35% - 85%, 7% - 40% and 7% - 45% whereas in our study these percentages were 50%, 26.6% and 23.3 % respectively.

The histological downgrading of recurrent tumors is unusual and was reported in 6 cases in the study of Tan et al.⁹ A likely explanation is insufficient sampling of recurrent lesions in that series. Pathological diagnosis of PTs can be difficult on cytology or small biopsy specimens. PTs are often heterogeneous and some areas of the tumor may be indistinguishable from fibroadenoma and a small biopsy may only sample these areas. Furthermore, biopsies of a malignant PT may include only the malignant stromal component of the tumor and a diagnosis of sarcoma may be rendered if the biphasic nature of the tumor is not appreciated.² Thus, confidence in correctly diagnosing the lesion is

significantly greater with excisional biopsy.¹¹

Standard therapy includes wide surgical excision with a margin of more than 1 cm even in benign tumors. Mastectomy is necessary only when tumor cannot be removed with adequate clearance. Most of the studies in the literature have found that a positive margin status is the most consistent indicator of local recurrence.^{9,12} Preoperative diagnosis is then important for good local control. The local recurrence in our study was seen in one case of benign tumor. This is comparable with other studies.^{9,13}

In a large series, total mastectomy for the malignant and borderline tumors had better results than breast conserving surgery. In that study, radiotherapy was an independent favorable prognostic factor for local control of the malignant and borderline group.¹⁴ Adjuvant systemic therapy is of no proven value.¹⁵ The recurrence rate reported in 19 studies on PTs varied widely (benign 1.5% - 12%, borderline 0% - 38.5% and malignant 3% - 50%) but has an upward trend with increasing grade.¹⁰ Our study also revealed overall metastatic rate of 10% (benign 0%,

borderline 3.3% and malignant 6.6%). The WHO reported an overall metastatic rate of 10% (benign 0%, borderline 4% and malignant 22%). The range of 5-years disease free survival is between 78% - 91 %.

CONCLUSIONS:

Phyllodes tumors of the breast have an unpredictable outcome. A wide local excision with adequate margin of normal breast tissue, is the preferred initial therapy.

REFERENCES:

1. Tavassoli FA, Devilee P, Eds. Pathology and Genetics of Tumours of the Breast and Female Genital Organs. In: World Health Organization Classification of Tumours. Lyon, France: IARC Press; 2003:99-103.
2. Abdel Krim SB, Tarbelsi A, Bouzrara M, Zaher M, Memmi A, Bakir DA, et al. Phyllodes tumor of the breast : A review of 26 cases. *Tunis J Surg.* 2010;129-34.
3. de Ross WK, Kaya P, Dent DM. Factors leading to local recurrence or death after surgical resection of phyllodes tumors of the breast. *Br J Surg.*1999;89:396-9.
4. Korula A, Varghese J, Thomas M, Vyas F. Malignant phyllodes tumour with intraductal and invasive carcinoma and lymph node metastasis. *Singapore Med J.* 2008;49:318-21.
5. Barrio AV, Clark BD, Goldberg JI, Hoque LW, Bernik SF, Flynn LW, et al. Clinicopathologic features and long-term outcomes of 293 phyllodes tumors of the breast. *Ann Surg Oncol.* 2007;14:2961-70.
6. Reinfuss M, Mitus J, Duda K, Stelmach A, Rys J, Smolak K. The treatment and prognosis of patients with phyllodes tumor of the breast: an analysis of 170 cases. *Cancer.* 1996;77:910-16.
7. Liberman L, Bonaccio E, Hamele-Bena D, Abramson AF, Cohen MA, Dershaw DD. Benign and malignant phyllodes tumors: mammographic and sonographic findings. *Radiology.* 1996;198:121-4.
8. Foxcroft LM, Evans EB, Porter AJ. Difficulties in the pre-operative diagnosis of phyllodes tumours of the breast: a study of 84 cases.

9. Tan PH, Jayabaskar T, Chuah KL, Lee HY, Tan Y, Hilmy M, Hung H, et al. Phyllodes tumors of the breast: the role of pathologic parameters. *Am J Clin Pathol.* 2005;123:529-40.
10. Karim RZ, Gerega SK, Yang YH, Spillane A, Carmalt H, Scolyer RA, Lee CS. Phyllodes tumours of the breast: a clinicopathological analysis of 65 cases from a single institution. *Breast.* 2009;18:165-70.
11. Lifshitz OH, Whitman GJ, Sahin AA, Yang WT. Radiologic- pathologic conferences of the University of Texas M.D. Anderson Cancer Center. Phyllodes tumor of the breast. *Am J Roentgenol.* 2003;180:332.
12. Taira N, Takabatake D, Aogi K, Ohsumi S, Takashima S, Nishimura R, et al. Phyllodes tumor of the breast: stromal overgrowth and histological classification are useful prognosis-predictive factors for local recurrence in patients with a positive surgical margin. *Jpn J Clin Oncol.* 2007;37:730-36.
13. Kraemer B, Hoffmann J, Roehm C, Gall C, Wallwiener D, Krainick-Strobel U. Cystosarcoma phyllodes of the breast: a rare diagnosis: case studies and review of literature. *Arch Gynecol Obstet.* 2007;276:649-53.
14. Belkacemi Y, Bousquet G, Marsiglia H, Ray-Coquard I, Magne N, Malard Y, et al. Phyllodes tumor of the breast. *Int J Radiat Oncol Biol Phys.* 2008;70:492-500.
15. Telli ML, Horst KC, Guardino AE, Dirbas FM, Carlson RW. Phyllodes tumors of the breast: natural history, diagnosis, and treatment. *J Natl Compr Canc Netw.* 2007;5:324-30.