SURGICAL MANAGEMENT OF PHYLLODES TUMORS OF BREAST

Original Article

MEMENİN FİLLODES TÜMÖRLERİNDE CERRAHİ TEDAVİ

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ABSTRACT

Objectives: Phyllodes tumors are rare breast tumors and challenges still exist in diagnosis and treatment. In this study we aimed to present our surgical approach and results of the patients with definitive diagnosis of phyllodes tumors.

Patients and Method: Medical records of thirteen patients with final pathology of phyllodes tumor who had been operated in Acıbadem Bakırköy, Maslak and International Hospital General Surgery Department between 2010 and 2013 were reviewed retrospectively. Demographic data along with clinicopathological features of the patients and type of surgery were analyzed.

Results: Median age of the patients with benign and borderline phyllodes tumors were 35 (24-47) and 31 (21-79), respectively. Median size of the tumor was 3.7cm (1.5-5.5cm) in the benign phyllodes groups and 5.2cm (2.4-12cm) in borderline phyllodes group. Ultrasonography, mammography and breast MRI was used in 13 (100%), 4(37%) and 2 (15.3%) patients, respectively. The majority of the patients underwent excisional biopsy for definitive diagnosis. Three patients (23%) were re-operated to achieve safe surgical margins. In pathological examination, 4 tumors were found to be borderline, and 10 tumors were found to be benign phyllodes tumors. There was no malignant phyllodes tumor. None of the patients has a local or systemic recurrence in a median follow-up of 12 (2-24) months.

Conclusıon: Wide excision with safe surgical margins is the preferred therapy

as well as it is necessary for precise diagnosis in phyllodes tumors of breast.

Key words: *Phyllodes tumor; breast; excisional biopsy;segmental mastectomy.*

ÖZET

Amaç: Fillodes tümörleri nadir görülen meme tümörleri olup tanı ve tedavisinde tartışmalar mevcuttur. Bu yazıda kesin tanısı fillodes tümör olan hastalardaki cerrahi yaklaşımımızı ve sonuçlarımızı sunmayı amaçladık.

Hastalar ve yöntem: Acıbadem Bakırköy, Maslak ve International Hastaneleri'nde 2010-2013 yılları arasında ameliyat edilen ve kesin tanısı fillodes tümör olan hastaların tıbbi kayıtları retrospektif olarak incelendi. Hastaların demografik ve klinikopatolojik özellikleri ile yapılan cerrahi tipi analiz edildi.

Sonuçlar: Hastaların median yaşı, benign ve borderline fillodes grubunda sırasıyla 35 (24-47) ve 31 (21-79) idi. Median tümör çapı benign fillodes grubunda 3.7cm(1.5-5cm) ve borderline grupta 5.2cm (2.4-12cm) idi. Onüç hastada (%100) ultrasonografi, 4 hastada (%37) mammografi ve 2 hastada (%15.3) meme MRI yapıldı. Kesin tanı için hastaların büyük çoğunluğunda eksizyonel biyopsi yapıldı. Üç hasta (%23) güvenli cerrahi sınırı sağlamak için ikinci kez ameliyat edildi. Patolojik incelemede 4 tümör borderline ve 10 tümör benign fillodes tümörü olarak değerlendirildi. Malign fillodes tumor saptanmadı. Median 12 ay (2-24) olan takip süresi sonunda hiç bir hastada local ya da sistemik nüks görülmedi.

Sonuç: Güvenli cerrahi sınır ile birlikte geniş eksizyon memenin fillodes tümörlerinin kesin tanısı için gereklidir ve tercih edilen tedavi yöntemidir.

Anahtar kelimeler: *Fillodes tümör; meme; eksizyonel biyopsi; segmental mastektomi.*

INTRODUCTION

Phyllodes tumors are rare biphasic fibroepithelial tumors. They constitute up to 0.3-0.5% of breast tumors (1-4). Women aged between 35 and 55 years are commonly involved (2,3,5). It was believed to be benign until 1943 when Cooper and Ackerman reported malignant biological potential (6). Today, the term "phyllodes tumor" is used and it is classified as benign, borderline or malignant according to histological features (7). The term phyllodes tumor represents a broad spectrum of fibroepithelial lesions. At one extreme there are malignant phyllodes tumors which have a propensity for rapid growth and metastatic potential (8,9,10). However, most common issue is local recurrence which is mostly affected by surgical management (2,10,11). The main problem is preoperative diagnosis. Mammography and ultrasonography are main imaging modalities as in other breast lesions. The value of fine needle aspiration biopsy (FNAB) is controversial whereas core needle biopsy has higher accuracy (12,13).

Surgery is the mainstay of treatment of phyllodes tumors (1-4,7-11). Lumpectomy with adequate surgical margins or segmental mastectomy is considered enough (3,9). Mastectomy can be done in patients with large or recurrent tumors and when breast conserving surgery is inappropriate for cosmetic reasons (14,15). The role of adjuvant chemotherapy and radiotherapy is uncertain for management of malignant phyllodes tumors (3,16).

PATIENTS AND METHOD

Patients with final pathology of phyllodes tumor who had been operated in Acıbadem Bakırköy, Maslak and International Hospital General Surgery Department between 2010 and 2013 were included in the study. All medical records were reviewed retrospectively. Demographic along with

clinicopathological features of the patients and type of surgery were analyzed. The pathological criteria used in classification of phyllodes tumors as benign, borderline or malignant were number of mitosis per 10 high power fields (HPF), stromal cellularity (minimal, moderate, marked), cellular atypia (minimal, moderate, marked), stromal overgrowth (minimal, moderate, marked), tumor necrosis and tumor margins (expansive/infiltrative). Surgical procedures were lumpectomy +/- re-excision, or segmental mastectomy or simple mastectomy with axillary dissection.

STATISTICAL ANALYSIS

Patients' age, size of the tumor, site of the tumor, primary surgery, secondary surgery (re-excision, segmental mastectomy), status of the surgical margins and local recurrence were recorded. The patients were classified as benign or borderline/malignant in two groups. Two groups were compared by means of age and tumor size by Mann Whitney-U test. P value <0.05 was considered statistically significant. Statistical analysis was performed by SPSS 15.0 (SPSS, Inc. Chicago, IL) software program.

RESULTS

There were 13 patients with a final pathological diagnosis of cystosarcoma phyllodes included in the study. One patient was operated twice with 9 months interval for development of phyllodes tumor in contralateral breast. This patient was included twice in the statistical analysis. Median age of the patients with benign and borderline phyllodes tumors were 35 (24-47) and 31 (21-79), respectively. The difference was not statistically significant (p=0.67). Median size of the tumor was 3.7cm (1.5-5.5cm) and 5.2cm (2.4-12cm) in benign and borderline phyllodes groups, respectively. The difference was not also statistically significant (p=0.11). The clinicopathological features and types of surgery are shown in **Table I**.

	Benign Phyllodes Tumor	Borderline Phyllodes Tumor	P value (Significance <0.05)
Number of breast lesions	10	4	-
Age of the patient (Median)	35 (24-47)	31 (21-79)	0.67
Tumor size	3.7cm	5.2cm	0.11
USG	10	4	
Lobulated borders	10	4	
Heterogenicity	3	1	
Hypervascularity	2	1	
Hypoechoic pattern	1		
Mammography	2	2	
MRI		0	
Lobulated mass	2		
Type II washout pattern of contrast	1		
Type III washout pattern of contrast	1		
FNAB	1 (Inconclusive)	0	
Core biopsy	1 (Inconclusive)	0	
Frozen section	3 (Conclusive)	0	
Primary surgical management			
Excisional biopsy +/- re-excision	7	1	
Segmental mastectomy	3	2	
Simple mastectomy + aksillary dissection	0	1	
Re-operation	2	1	

Table I. *Demographic, clinicopathological features of the patients and types of surgical management.*

All patients had breast ultrasonography, whereas 4 patients (37%) had mammogram and 2 patients (15.3%) had breast MRI. The majority of the patients underwent excisional biopsy for definitive diagnosis. FNAB was attempted in one patient and core needle biopsy was done in one patient for preoperative diagnosis. However, discrimination between fibroadenoma and phyllodes tumor could not be made in both of these patients, and a surgical excisional biopsy was needed for definitive diagnosis. In patients who eventually underwent excisional biopsy, frozen section was done in only three patients and re-excision with wider margins was performed after peroperative diagnosis of phyllodes tumor. Three

patients (23%), who underwent lumpectomy, were re-operated for positive margins or inadequate margins, and reexcisions were performed for wider margins. Modified radical mastectomy was performed in only one patient with a 12cm tumor.

In pathological examination, 4 tumors were found to be borderline, and 10 tumors were found to be benign phyllodes tumors. There was no malignant phyllodes tumor. Tumors were located in left breast in 8 patients and in right breast in 4 patients and in both sides in one patient. None of the patients received adjuvant radiotherapy or systemic chemotherapy. None of the patients has a local or systemic recurrence in a median follow-up of 12 (2-24) months.

DISCUSSION

Phyllodes tumors of the breast are rarely seen and constitute less than 1% all cases (1-4). Fibroepithelial tumors with a wide range of histological features are classified as phyllodes tumor and pathological findings are not necessarily consistent with the clinical course (4). Preoperative diagnosis, surgical management strategy, follow-up, and adjuvant therapy all have been challenging because of rarity of these tumors and differences in management in various centers. The problem is local recurrence ranging between 10-40%, latent malignancy and metastatic disease reported about 10 % overall (3-6,10,17).

The most important issue to prevent local recurrence is to achieve wide surgical margins (2,10,18,19). However, it is often hard to diagnose phyllodes tumors preoperatively because the clinical appearance and physical findings are quite similar to that of fibroadenoma (20). Definitive diagnosis is usually made after pathological examination of the specimen. Ultrasonography (USG), mammography and magnetic resonance imaging (MRI) are used in diagnosis of phyllodes tumors as in other breast lesions. Ultrasonographic appearance of these lesions is similar to fibroadenomas (8). They are seen as lobular shaped, well circumscribed masses with low level homogeneous internal echoes (21,22). Posterior acoustic shadowing, ill defined margins and hypervascularity can be seen in color Doppler USG. Mammography shows oval or lobulated mass with rounded borders. A radiolucent halo and coarse calcifications may be seen (21,23). MRI findings of phyllodes tumors are round or lobulated shape with heterogeneous internal structure which exhibits hypointense signals on T1-weighed images and hyper/isointense signals on T2-weighed images with different contrast enhancement patterns (24).

USG was performed in all our patients. Solid mass with lobulated borders was the common finding in all cases. Heterogeneity was noted in four patients, hypervascularity was noted in three and hypoechoic pattern was noted in one patient. Rapid growth of a pre-existing lesion was seen 3 patients. Mammographic findings in 4 patients were consistent with other reports which showed lobulated mass lesion showing progression in follow-up. In one patient MRI showed a hypointense lesion in T2 weighed images with type III wash out pattern. The other lesion showed type II wash out pattern of the contrast material and was hyperintense in T2 weighed images. These lesions turned out to be benign phyllodes tumors.

Fine needle aspiration biopsy has been reported to be correct about 23-25% of the cases (12-14). Core needle biopsy has been reported to be more precise due to more extensive tissue sampling compared to fine needle aspiration biopsy (12-14). In a series by Taira et al, correct preoperative diagnosis in phyllodes tumors has been reported to be 31% (4). In our cases FNAB and core needle biopsy were used in only two patients but the discrimination between a proliferative fibroadenoma and phyllodes tumor could

not be made. All patients in our series eventually underwent an excisional biopsy for definitive histopathological diagnosis. Peroperative frozen section was done in 3 patients and lumpectomy with wide margins were performed.

Surgical management of phyllodes tumors has still been a challenge (25). Since these tumors are seen rarely and due to different surgical approaches between centers which have been reported can vary among series. Wide local excision is usually accepted to be adequate because these tumors tend to be solitary. Mastectomy is usually recommended for tumors larger than 10cm, or locally recurrent tumors, in whom breast conserving surgery is not acceptable for cosmetic reasons, and for malignant phyllodes tumors (14,15).

Primary route of metastasis is hematogenous (14), however axillary involvement has also been reported to be approximately 2% (10). Axillary dissection is usually performed in less than 10% of the cases (12,14,20). Axillary dissection has been performed in one patient in our series with simple mastectomy. The axillary lymph nodes were negative for metastasis consistent with other reports.
Phyllodes tumors are classified as benign, borderline and malignant on histological basis. However, there is a broad spectrum of fibroepithelial lesions in this category and it is difficult to determine the exact category which a phyllodes tumor fits (5).The clinical behavior of the tumor is often unpredictable, although it is known that aggressiveness and metastatic potential increases with the age of the patient and size of the tumor increases (14). Benign lesions are seen in younger patients whereas borderline and malignant lesions are usually seen in the elderly. In our series, even though patients in borderline group were older with a larger tumor size compared to the benign phyllodes group, these differences between 2 groups did not reach a statistically significant level. This is probably due to small number of patients in this series.

It has been shown that the cell type that possesses metastatic potential is the stromal cells. Thus microscopic appearance and abundance of stromal cells are critical for malignant behaviour (4,9.17). Follow up of the patients with phyllodes tumors is important to detect local recurrence or distant metastasis. For the first 2 years, clinical examination with radiological imaging is recommended every 6 months (6). Age of the patient, tumor size, surgical approach, mitotic activity, stromal overgrowth and surgical margin have been reported to be important prognostic factors for local recurrence (4,10,17). No local recurrence or distant metastasis developed in patients in our series. However, progression of a pre-existing lesion in the contralateral breast resulted in a patient with a benign phyllodes tumor.

CONCLUSION

Excisional biopsy is required for definitive diagnosis of patients with phyllodes tumor. Surgery as segmental mastectomy with wide margins or mastectomy is the mainstay therapy for the majority of the patients whereas the efficacy of adjuvant therapies has not been proven by far.

REFERENCES

1)Rowell MD, Perry RR, Hsiu JG, Barranco SC. Phyllodes tumors. Am J Surg 1993;165:376-9.

2)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;77:910-6.

3)Chaney AW, Pollack A, McNeese MD, et al. Primary treatment for cystosarcoma phyllodes of the breast. Cancer 2000;89:1502-11.

4)Taira N, Takabatake D, Aogi K, 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;37:730-6.

5)Chen WH, Cheng SP, Tzen CY, et al. Surgical treatment of phyllodes tumors of the breast: Retrospective review of 172 cases. J Surg Oncol 2005;91:185-194.

6)Mishra SP, Tiwary SK, Mishra M, Khanna AK. Phyllodes tumor of breast. ISRN Surgery 2013;2013:361469.doi: 10.1155/2013/361469. Epub 2013 Mar 20.

7)Anonymous: The World Health Organization histological typing of breast tumors-second edition. The World Organization. Am J Clin Pathol 1982;78:806-16.

8)Parker SJ, Harries SA. Phyllodes tumors. Postgrad Med J 2001;77:428-35.

9)Kapiris I, Nasiri N, A'Hern R, Healy V, Gui GP. Outcome and predictive factors of local recurrence and distant metastasis following primary surgical treatment of high-grade malignant phyllodes tumors of the breast. Eur J Surg Oncol 2001;27:723-30.

10)Asoğlu O, Uğurlu MM, Blanchard K, et al. Risk factors for recurrence and death after primary surgical treatment of malignant phyllodes tumors. Ann Surg Oncol 2004;11:1011-1017.

11)Salvadori B, Zurrida SM, Clemente C. Phyllodes tumors. Am J Surg 1993;165:376-9.

12)Jacklin RK, Ridgway PF, Ziprin P, Healy V, Hadjiminaz D, Darzi A. Review: optimising preoperative diagnosis in phyllodes tumour of the breast. J Clin Pathol 2006;59:454-9.

13)Foxcroft LM, Evans EB, Porter AJ. Difficulties in the preoperative diagnosis of phyllodes tumors of the breast: a study of 84 cases. The Breast 2007;16:27-37.

14)Verma S, Singh RK, Rai A, Pandey Cp, Singh M, Mohan N. Extent of surgery in management of phyllodes tumor of the breast: A retrospective multicenter study from India. J Cancer Res Ther 2010;6:511-5.

15)Singh G, Sharma RK. Immediate breast reconstruction for phyllodes tumors. Breast 2008;17:296-301.

16)Morales-Vasquez F, Gonzalez-Angulo A, Broglio K, et al. Adjuvant chemotherapy with doxorubicine and dacarbazine has no effect in recurrence free survival of malignant phyllodes tumors of the breast. The Breast Journal 2007;13:551-6.

17)PandeyM, Mathew A, Kattoor J, et al. Malignant phyllodes tumor. Breast J 2001;7:411-6.

18)Bennett IC, Khan A, De Freitas R. Phyllodes tumors: A clinicopathological review of 30 cases. Aust N Z J Surg 1992;62:628-33.

19)Bhargav PV, Mishra A, Agrawal G, Agrawal A, Verma AK, Mishra SK. Phyllodes tumour of the breast: Clinicopathological analysis of recurrent vs nonrecurrent cases. Asian J Surga 2010;32:224-8.

20)Cabıoğlu N, Çelik T, Özmen V, et al. Memenin filloides tümörlerine tedavi yaklaşımları. Meme Sağlığı Dergisi 2008;4(2):99-104.

21)Feder JM, De Parades ES, Hogge JP, Wilken JJ. Unusual breast lesions: radiologic-pathologic correlation. Radiographics 1999;19:11-26.

22)Beuglet CC, Soriano R, Kurtz AB. Ultrasound, X-ray mammography, and histopathology of cystosarcoma phylloides. Radiology 1983:146;481-6.

23)Jorge Blanco A, Vargas Serrano B, Rodriguez Romero R, Martinez Cendejaz E. Phyllodes tumors of the breast. Eur Radiol 1999;9:356-60.

24)Yabuuchi H, Soeda H, Matsuo Y, et al. Phyllodes tumor of the breast: Correlation between MR findings and histologic grade. Radiology 2006;241:702-9.

25)Cheng SP, Chang YC, Liu TP, Lee JJ, Tzen CY, Liu CL. Phyllodes tumor of the breast: the challenge persists. World J Surg 2006;30:1414-21.