

Therapeutic Approachs To Breast Phyllodes Tumor

Fatih Altıntoprak¹, Taner Kivılcım², Osman Nuri Dilek¹

ABSTRACT

Phyllodes tumors are very rare tumors of the breast. They usually present in fast-growing mass form and are confused with diagnosis of fibroadenoma in daily clinical practice. The adequacy of treatment and follow-up may be hesitated in some centers which are not engaged with breast disease spesifically due to post-surgical excisional diagnosis in usual. In this article, we have reviewed the treatment options of phyllodes tumors of the breast.

Key words: Breast, phyllodes tumor, cystosarcoma phyllodes

Meme Filloides Tümörlerine Tedavi Yaklaşımları

ÖZET

Filloides tümörler memenin oldukça nadir görülen tümörlerindedir. Genellikle hızlı büyüyen kitle şikayeti ile ortaya çıkarlar ve klinik pratikte sıklıkla fibroadenom ile karıştırılırlar. Bu nedenle genellikle cerrahi eksizyon sonrası tanı koyulduğu için meme hastalıkları ile spesifik olarak ilgilenmeyen merkezlerde tedavi yeterliliği ve klinik takip konularında tereddütler oluşabilmektedir. Bu yazıda memenin filloides tümörlerinin tedavi seçeneklerini kısaca gözden geçirdik.

Anahtar kelimeler: Meme, filloides tümör, sistosarkom filloides

Frequency and Terminology

Phyllodes tumors are rare neoplasms accounting for 0.3% - 0.9% of all malignant breast neoplasms and 2-3% of all fibroepithelial tumors (1) When cystosarcoma phyllodes was first described by Müller in 1838, the term 'sarcoma' was used because of the sarcoma-like macroscopic findings of this tumor rather than to indicate its malignant potential (2). In fact, the reality that this entity possessed a malignant potential was clearly realized in 1931 when the first metastatic phyllodes tumor was reported (3). In 1981, the World Health Organization (WHO) defined this rare breast neoplasm as "phyllodes tumor" and classified it into three subgroups as "benign (35-64 %)", "borderline", and "malignant" according to their histopathological findings and the number of mitosis.

Despite its high incidence among women of the ages of 35 to 55, (4) these neoplasms can also be detected in adolescents,(5) and also rarely in men (6).

Clinical Findings

In general, phyllodes tumors clinically presents as a rapidly growing and clinically benign (non-tender, well shaped and mobile) breast lump and usually noticed by the patient himself. They may grow rapidly in some cases leading to the onset of a number of particular findings such as a bright thin skin, ulcerations due to ischemia and tenderness. However, these findings may also accompany another benign mass of the breast which is the fibroadenoma. Thus, it is obvious that clinical findings

¹Sakarya University Faculty of Medicine, Department of General Surgery, ²Sakarya University Research and Educational Hospital, Department of General Surgery

Correspondence: Fatih Altıntoprak, Sakarya University Faculty of Medicine Department of General Surgery
GSM: +90 533 548 34 15 e-mail: fatihaltintoprak@yahoo.com

are insufficient for the differential diagnosis between malignant and benign disease (7-9). Kapisir et al. (10) reported that rapid tumoral growth was detected in 43% of the patients, whereas this rate was found to be 24% according to Hassouna et al. (4) although pain related to a phyllodes tumor is not a frequent complaint, there are studies that report tenderness as the cause of admission to the hospital, (4) and there are also other studies emphasizing that the survival rates of the patients presenting with tenderness are lower (11).

TREATMENT OPTIONS

Surgical Treatment

Wide surgical excision in order to obtain clear surgical margins is the first choice of treatment, and axillary dissection is unnecessary. In contrast to the performed mastectomies in the past, the current surgical approach to this entity advocates a more breast preserving modality via surgical excision with tumor-free clear surgical margins. Mastectomy should be reserved for special indications such as local recurrence, gross tumors (>10 cm), inappropriate tumor-breast ratio, and cases in which tumor-free surgical margins are impossible to be achieved. The excisions must be carried out with the effort to obtain at least a 1 - 2 cm tumor-free distance from the surgical margins (10,12-23). In their study, Mangi et al (20) reported that this distance was less than 1 cm in all cases of local recurrences, and De Roos et al. (22) stated that all local recurrences were the outcomes of insufficient primary surgery having left positive surgical margins in the initial operations.

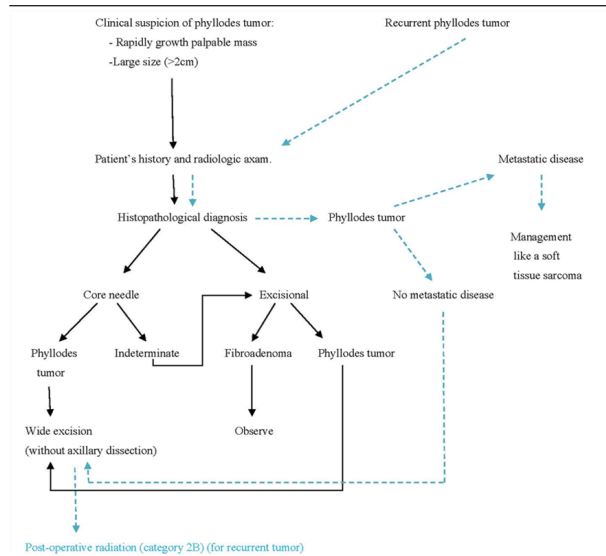
In another study of Fou et al. (23), it was reported that following local excisions the local recurrence rate was 24%, and the distant metastasis rate was 6% whereas these rates were found to be 0%, and 33% consecutively in patients having undergone mastectomies leading the authors to the suggestion that the treatment for this disease could be accomplished by local excisions with clear surgical margins instead of performing mastectomies. In their study on three groups of patients having undergone local excision in the first, extended local excision in the second, and mastectomy in the third group, Chen et al. (24). reported their local control rates to be 88.7%, 88.2%, and 100% consecutively. They have also stated that since local excision ended up with higher rates of surgical margin positivity (18%), extended lo-

cal excision could be the preferred choice of primary surgical treatment. On the other hand, according to Guerrerol et al. (25) even gross tumors can be treated with local excision, as long as a 2 cm clear surgical margin is possible to be obtained, and as long as there won't be any significant cosmetic problems. Kapisir et al. (10) reported that the factors effecting local recurrence and distant metastasis are tumor size and surgical margin, while Pandey et al. (26) also reported that the only prognostic factor found to be statistically significant for the 5-year disease-free survival rates was the achievement of tumor-free clear surgical margins in the initial surgical interventions.

Since the phyllodes tumors spread through the bloodstream for metastasis, the lymph node metastasis rates are very low (<5%). Thus, axillary dissection is unnecessary during the initial surgical intervention. Axillary dissection is only indicated for cases having presented with a palpable axillary lymph node, (4,10,24-27) or the intraoperative detection of a lymph node metastasis via frozen section (7). However, Cedermark et al. (28) reported that despite the presence of a palpable axillary lymph node at the time of admission in patients with the diagnosis of the phyllodes tumor of the breast, in fact, only 1% was found to be pathologic and the remaining majority was determined as reactive lymph nodes.

Chemotherapy, Radiotherapy and Hormonal Therapy

Because of the limited number of cases, there still is not a consensus about the indications of adjuvant therapy methods. Although a number of studies are present reflecting better survival outcomes of radiotherapy (RT) for malignant phyllodes tumors, (26,29) it is not routinely used currently, and is suggested for its use in cases of local recurrence, symptomatic metastatic disease, thoracic wall invasions and according to histologic criteria (Table 1) (25,30). While the epithelial component of most phyllodes tumors contains oestrogen receptors (58%) and/or progesterone receptors (75%), endocrine therapy has no proven role in the treatment of phyllodes tumors (31). Similarly, there is no evidence that adjuvant cytotoxic chemotherapy (CT) provides a benefit in reducing recurrences or death. There are also studies revealing the preventive effects of ifosfamide and/or doxorubicine based chemotherapy protocols on systemic metastases,(32) but this subject is also disputatous and forthcoming studies are still required.

Table 1. Treatment algorithm for breast phyllodes tumor*

*The preparation of this algorithm is based on the NCCN Guideline 2011

Chemotherapy and radiotherapy are reserved for only selected cases including local recurrence, insufficiency of the initial surgical treatment, and/or metastatic disease (4,10,24-27,32,33). Local recurrences are the most common recurrence type for phyllodes tumors. Positive surgical margins, fibroproliferation in the surrounding breast tissue, and necrosis are associated with a markedly increase in local recurrence rates. The lung is the most distant recurrences area (17). Patients with stromal overgrowth, particularly when the tumor size was > 5 cm, were found to have a high rate of distant failure. 31 Death from phyllodes tumor is rare (2%), and only phyllodes tumors that demonstrate uniformly aggressive pathologic features seem to be associated with mortality (21). In conclusion, it can be stated that the phyllodes tumors of the breast are rare neoplasms and the first choice of preference for treatment is surgical excision with tumor-free clear surgical margins. RT and CT are reserved for elected cases with specific indications. Although the most frequent diagnosis of rapidly growing masses of the breast in adolescents is fibroadenoma, the phyllodes tumor must also be kept in mind for differential diagnosis in such cases. Since these tumors are rare, and because of the lack of a consensus on the appropriate treatment modality for these neoplasms, such cases must be referred to highly experienced specific institutions when encountered.

REFERENCES

1. Kario K, Maeda S, Mizuno Y, Makino Y, Tankawa H, Kitazawa S. Phyllodes tumor of the breast: a clinicopathologic study of 34 cases. *J Surg Oncol* 1990;45(1):46-51.
2. Muller J. *Ueber den feineren Bau und die Form der Krankhaften Geschwülste*. Berlin: G Reimer, 1838
3. Lee B, Pack G. Giant intracanalicular fibroadenomyoma of the breast. The so-called cystosarcoma phyllodes mammae of Johannes Muller. *Am J Can* 1931;93(1):250-68.
4. Ben Hassouna J, Damak T, Gamoudi A, et al. Phyllodes tumors of the breast: a case series of 106 patients. *Am J Surg* 2006;192(2):141-7.
5. Stebbing JF, Nash AG. Diagnosis and management of phyllodes tumour of the breast: experience of 33 cases at a specialist centre. *Ann R Coll Surg Engl* 1995;77(3):181-4.
6. Nielsen VT, Andreasen C. Phyllodes tumor of the male breast. *Histopathology* 1987;11(7): 761-2.
7. Pietruszka M, Barnes L. Cystosarcoma phyllodes: a clinicopathologic analysis of 42 cases. *Cancer* 1978;41(5): 1974-83.
8. Kario K, Maeda S, Mizuno Y, Makino Y, Tankawa H, Kitazawa S. Phyllodes tumor of the breast: a clinicopathologic study of 34 cases. *J Surg Oncol* 1990; 45(1):46-51.
9. Gatta G, Iaselli F, Parlato V, Di Grezia G, Grassi R, Rotondo A. Differential diagnosis between fibroadenoma, giant fibroadenoma and phyllodes tumour: sonographic features and core needle biopsy. *Radiol Med* 2011;116(6):905-18.
10. Kapiris I, Nasiri N, A'Hern R, Healy V, Gui GP. Outcome and predictive factors of local recurrence and distant metastases following primary surgical treatment of high-grade malignant phyllodes tumours of the breast. *Eur J Surg Oncol* 2001; 27(8):723-30.
11. Roa JC, Tapia O, Carrasco P, et al. Prognostic factors of phyllodes tumor of the breast. *Pathol Int* 2006;56(6):309-14.
12. 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(5): 910-6.
13. Verma S, Singh RK, Rai A, Pandey CP, Singh M, Mohan N. Extent of surgery in the management of phyllodes tumor of the breast: a retrospective multicenter study from India. *J Cancer Res Ther* 2010;6(4):511-5.
14. Tan PH, Thike AA, Tan WJ, et al. Predicting clinical behaviour of breast phyllodes tumours: a nomogram based on histological criteria and surgical margins. *J Clin Pathol* 2012; 65(1):69-76.
15. Guillot E, Couturaud B, Rey F, et al. Management of phyllodes breast tumors. *Breast J* 2011;17(2):129-37.
16. Akin M, Irkorucu O, Koksall H, et al. Phyllodes tumor of the breast; a case series. *Bratisl Lek Listy* 2010;111(5):271-4.
17. Khosravi-Shahi P. Management of non metastatic phyllodes tumors of the breast: review of the literature. *Surg Oncol* 2011;20(4):e143-8.
18. Parker SJ, Harries SA. Phyllodes tumors. *Postgrad Med J* 2001; 77(909):428-35.

19. Chaney AW, Pollack A, McNeese MD, et al. Primary treatment of cystosarcoma phyllodes of the breast. *Cancer* 2000;89(7):1502-11.
20. Mangi AA, Smith BL, Gadd MA, Tanabe KK, Ott MJ, Souba WW. Surgical management of phyllodes tumors. *Arch Surg* 1999; 134(5):487-92.
21. Salvadori B, Cusumano F, Del Bo R, et al. Surgical treatment of phyllodes tumors of the breast. *Cancer* 1989; 63(12):2532-6.
22. De Roos WK, Kaye P, Dent DM. Factors leading to local recurrence or death after surgical resection of phyllodes tumors of the breast. *Br J Surg* 1999;86(3):396-9.
23. Fou A, Schnabel FR, Hamele-Bena D, et al. Long-term outcomes of malignant phyllodes tumors patients: an institutional experience. *Am J Surg* 2006;192(4):492-5.
24. 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(3):185-94.
25. Guerrero MA, Ballard BR, Grau AM. Malignant phyllodes tumor of the breast: review of the literature and case report of stromal overgrowth. *Surg Oncol* 2003;12(1):27-37.
26. Pandey M, Mathew A, Kattoor J, et al. Malignant phyllodes tumor. *Breast J* 2001;7(6):411-6.
27. Asoglu O, Ugurlu MM, Blanchard K, et al. Risk factors for recurrence and death after primary surgical treatment of malignant phyllodes tumors. *Ann Surg Oncol* 2004; 11(11):1011-7.
28. Cohn-Cedermark G, Rutqvist LE, Rosendahl I, Silfversward C. Prognostic factors in cystosarcoma phyllodes. A clinicopathologic study of 77 patients. *Cancer* 1991;68(9):2017-22.
29. Barth RJ, Wells WA, Mitchell SE, Cole BF. A prospective, multi-institutional study of adjuvant radiotherapy after resection of malignant phyllodes tumors. *Ann Surg Oncol* 2009;16(8):2288-94.
30. Belkacemi Y, Bousquet G, Marsiglia H, et al. Phyllodes tumor of the breast. *Int J Radiat Oncol Biol Phys* 2008;70(2):492-500.
31. Reimer T. Management of rare histological types of breast tumors. *Breast Care (Basel)* 2008;3(3):190-6.
32. McDonald OK, Lee CM, Tward JD, Chappel CD, Gaffney DK. Malignant phyllodes tumor of the female breast: association of primary therapy with cause-specific survival from the Surveillance, Epidemiology, and End Results (SEER) program. *Cancer* 2006;107(9):2127-33.
33. Morales-Vasquez F, Gonzalez-Angulo AM, Broqlio K, et al. Adjuvant chemotherapy with doxorubicin and dacarbazine has no effect in recurrence-free survival of malignant phyllodes tumors of the breast. *Breast J* 2007;13(6):551-6.