



Phyllodes Breast Tumors: A Review of a Single Saudi Institution Experience

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Abstract

Introduction: Phyllodes Tumors (PT) are rare fibroepithelial neoplasms, accounting for less than 0.5% of all primary breast tumors. This study aims to evaluate the local recurrence, distant metastasis, and mortality rates of PT cases.

Methods: A retrospective analysis of the clinical, pathological, and therapeutic data of 45 patients with a PT who were treated between January 2000 and December 2015 at a single Saudi institution. Tumors were classified into benign (21 cases), borderline (6 cases), and malignant (18 cases) according to the criteria proposed by the World Health Organization "WHO".

Results: The median follow-up period was 35 (7 months to 185 months). The median age was 37 (19 years to 62 years). The median tumor size was 9.2 (2.3 cm to 25 cm). Surgery consisted of wide local excision in 27 cases (60%), simple mastectomy in 14 cases (31.1%), and nipple-sparing mastectomy in 4 cases (8.9%). The surgical margins were positive in 12 cases (26.7%). While, the overall rate of local recurrence for the entire group was 8.9% (4 cases), it was 4.8% (1 case) for benign PT, and 16.7% (3 cases) for malignant PT. Distant metastasis developed in 6 patients with malignant PT; thus the distant metastasis rate was 13.3% for the entire group and 33.3% for the group with malignant PT. There were 2 mortality cases among those affected with malignant PT. Therefore, the mortality rate was 4.4% for the entire group and 11.1% for the group with malignant PT.

Conclusion: Our experience suggests that surgery with negative margins is the treatment of choice.

Keywords: Phyllodes tumors; Breast; Benign; Malignant

Introduction

Phyllodes Tumors (PTs) are rare fibroepithelial neoplasms, accounting for less than 0.5% of all primary breast tumors, and 2% to 3% of all fibroepithelial breast lesions [1]. Histologically PTs are biphasic, composed of a connective tissue stroma with epithelial elements, characterized by a heterogeneous morphological pattern and an unpredictable clinical behavior [1,2]. Phyllodes tumor is not a single disease entity but a heterogeneous disease, with a wide spectrum of clinical and pathological features [1]. Benign PTs have a local recurrence rate of 15%; whereas, malignant PT are aggressive tumors which associated with a distant metastasis rate of 10% [2]. Benign PT are similar to fibroadenomas and are difficult to distinguish from each other on clinical and radiological basis [3]. The diagnosis by core needle biopsy of a fibroadenoma at one end of the spectrum and malignant PT at the other end is usually straightforward. However, the distinction between a fibroadenoma with cellular stroma and benign PT, or borderline PT can present a serious diagnostic challenge and may not be possible on core needle biopsy [4]. Therefore, only complete excision can establish a definitive diagnosis and discriminate between the different types of PT [4]. This study aims to examine the clinical management of all the cases of PT treated over a 15 year period between January 2000 and December 2015 at King Faisal Specialist Hospital and Research Center (KFSH&RC), Riyadh, Saudi Arabia. In addition, it aims to evaluate the rate of local recurrence, the distant metastasis rate, the

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Table 1: Patients characteristic and surgical outcome.

	Total 45	Benign 21 (46.7%)	Borderline 6 (13.3%)	Malignant 18 (40%)	P value
Tumor size					
< 5 cm	13 (28.9%)	9 (42.9%)	0 (0%)	4 (22%)	0.19
5–10 cm	15 (33.3%)	7 (33.3%)	3 (50%)	5 (28%)	
> 10 cm	17 (37.8%)	5 (23.8%)	3 (50%)	9 (50%)	
Type of Surgery					
WLE	27 (60%)	17 (81%)	2 (33.3%)	8 (44.4%)	0.037
SM	14 (31.1%)	4 (19%)	3 (50%)	7 (38.9%)	
SSM	4 (8.9%)	0 (0%)	1 (16.7%)	3 (16.7%)	
Positive Surgical Margins	12 (26.7%)	6 (28.6%)	0 (0%)	6 (33.3%)	0.519
Adjuvant Therapy					
Chemotherapy	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.519
Radiation	3 (6.7%)	0 (0%)	0 (0%)	3 (16.7%)	
Local Recurrence	4 (8.9%)	1 (4.8%)	0 (0%)	3 (16.7%)	0.342
Distant Recurrence	6 (13.3%)	0 (0%)	0 (0%)	6 (33.3%)	0.005
Mortality	2 (4.4%)	0 (0%)	0 (0%)	2 (11.1%)	0.406
Adjuvant Chemotherapy	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1
Adjuvant Radiotherapy	3 (6.6%)	0 (0%)	0 (0%)	3 (16.7%)	0.1

WLE: Wide Local Excision; SM: Simple Mastectomy; SSM: Skin Sparing Mastectomy

mortality rate and overall survival rate.

Methods

A review of a retrospective database was performed on all patients diagnosed to have Phyllodes Tumor (PT) at King Faisal Specialist Hospital and Research Center (KFSH&RC), between January 2000 and December 2015. KFSH&RC is a tertiary referral hospital in Riyadh, Saudi Arabia. Data collected included age, presenting symptom, duration of symptoms, side and quadrant of disease, tumor size, histological type, surgical margins, and type of surgery. Follow-up data collected included the rate of local recurrence, distant metastasis, and mortality. The diagnosis of PT was confirmed by complete excision and pathological examination. Tumors were classified pathologically according to the criteria proposed by the World Health Organization "WHO" into 21 benign cases (46.7%), 6 borderline cases (13.3%), and 18 malignant cases (40%) [5]. One pathologist reviewed all the 45 cases, and the negative margin was defined as "no tumor on ink". However, an attempt was made to achieve a one cm safety margin during a Wide Local Excision "WLE". The study was approved by the institution's ethics and research committee. All statistical calculations were completed using SPSS statistical software, version 12. Continuous data was reported as median and range, categorical data was reported as absolute values and percentages. For group comparison differences between continuous data was compared using an unpaired Student's test and categorical data was compared using a chi-square test. A p value of 0.05 was considered to be a statistical significance level.

Results

Forty-five patients were diagnosed to have PT from 2000 until 2015 at KFSH&RC. All patients were females with a median follow-up period of 35 months (range 7-185). Twenty-one (46.7%) cases were benign, while 6 (13.3%) cases were borderline cases, and 18 were malignant cases (40%). The median age at the time of diagnosis was 38 years (range 19-62). The median age for benign was 35.2 years

(19-47), for borderline was 37.8 year (28-46), and for malignant PT was 37.7 years (24-62). Forty (88.9%) cases were premenopausal. The main complaint was a breast mass in all the cases (100%). The median duration of the symptoms was 9 months (range 2-180). The majority of the tumors occurred in the upper outer quadrant 27 cases (60%). Moreover the right breast was affected more frequently 32 cases (71%). Mammography and breast ultrasound were performed to evaluate the size and the extent of disease. Mammography or breast ultrasound or both were employed in all the patients, and the majority was reported as BIRADS 2 or 3. In addition, both images were nonspecific and unreliable in distinguishing fibroadenomas from PT. The median tumor size was 9.2 cm (range 2-25). The tumor size was less than 5 cm in 13 cases (28.9%), larger than 5 cm in 32 cases (71.1%), and larger than 10 cm in 17 cases (37.8%, Table 1). More than half the tumors larger than 5 cm were either borderline or malignant PT, 20 cases (62.5%). Among the malignant PT, the size was larger than 5 cm in 14 cases (77.8%, Table 1). The type of surgical procedure was based on the histologic subtype of PT and the size of the tumor. Surgery consisted of wide local excision in 27 cases (60%; 17 benign, 2 borderline, 8 malignant), simple mastectomy in 14 cases (31.1%; 4 benign, 3 borderline, 7 malignant), and nipple sparing mastectomy in 4 cases (8.9%; 1 borderline, 3 malignant; Table 1). The median tumor size for patients who underwent a WLE was 6.9 cm, and was 12.6 cm for patients who had a mastectomy (Table 2). None of our patients had a sentinel node biopsy or an axillary lymph node dissection or a frozen section. In addition, none of our patients was treated with systemic therapy. The surgical margins were positive in 26.7% (12 cases), and negative in 73.3% (33 cases). The margins were positive in 6 (28.6%) benign PT and 6 (33.3%) malignant PT. None of our patients with a positive margin was exposed to a re-excision. The surgeons explained the final pathology results to those patients and a re-excision option had been offered for those patients with a benign disease, but patients preferred a close observation with possibility of another surgery if the tumor recurs. However, for those patients who had a malignant PT with positive margins; 3 cases (16.7%) had a

Table 2: The clinical outcome in relation to age, tumor size, type of histology, type of surgery and surgical margin status.

	Local Recurrence N= 4	Distant Metastasis N= 6	Mortality Rate N= 2
Type of PT			
Benign	1 (25%)	0 (0%)	0 (0%)
Borderline	0 (0%)	0 (0%)	0 (0%)
Malignant	3 (75%)	6 (100%)	2 (100%)
Tumor Size			
<5cm	1 (25%)	0 (0%)	0 (0%)
5-10cm	1 (25%)	2 (33.3%)	0 (0%)
>10cm	2 (50%)	4 (66.7%)	2 (100%)
Type of Surgery			
WLX	4 (100%)	3 (50%)	1 (50%)
SM	0 (0%)	3 (50%)	1 (50%)
SSM	0 (0%)	0 (0%)	0 (0%)
Margin Status			
Positive (N=21)	1 (25%)	1 (16.7%)	0 (0%)
Negative (N=21)	3 (75%)	5 (83.3%)	2 (100%)

WLE: Wide Local Excision; SM: Simple Mastectomy; SSM: Skin Sparing Mastectomy

positive anterior margin (the skin) which had already removed with the surgical specimens. The other 3 cases (16.7%) had positive foci at the ink of the deep margin, so they received a radiation therapy. The overall rate of local recurrence for the entire group was 8.9% (4 cases). The rate of local recurrence was 4.8% for benign PT (one case), 0% for borderline PT, and 16.7% (3 cases) for malignant PT (Table 2). The incidence of local recurrence among patients having a wide local excision was 14.8% (4 out of 27 cases). But the incidence of local recurrence among patients with malignant PT following a wide local excision was 37.5% (3 out of 8 patients). All three local recurrences underwent initially a wide local excision, and all were salvaged with a simple mastectomy. The time to local recurrence for these three cases ranged from 6 to 24 months (Table 2). Distant metastasis to the bone and lung developed in 6 patients with malignant PT. Thus the distant metastasis rate was 13.3% for the entire group and 33.3% for malignant PT (Table 2). There were two mortality cases among those affected with malignant PT. Hence, the mortality rate was 4.4% for the entire group and 11.1% for the group with malignant PT. The overall survival rate for the entire group was 91.1% at 15 years.

Discussion

Phyllodes tumors occur almost exclusively in women, only a few cases have been reported in men [6]. Phyllodes tumors are very rare in children and only two cases of malignant PT have been reported [7,8]. The median age of our study population was 38 years which is consistent with other reports in the literature [9]. This age is 10 years to 15 years older than that reported for patients with fibroadenomas [6]. The majority of our patients presented late with tumors larger than 5 cm (71.1%) and the average duration of symptoms was 9 months. While, the clinical presentation varied among our patients; all our patients presented with a discrete painless mobile breast mass, and was difficult to differentiate clinically from a fibroadenoma. Imaging studies (mammography and ultrasound) were performed to assess the size and extent of disease and to exclude invasive ductal carcinoma. Our experience suggests that both studies are nonspecific and unreliable in distinguishing fibroadenomas from PT, nor can they predict the histologic subtype of PT, a finding consistent with that reported by others [10]. Our ratio of benign 21 cases (46.7%),

borderline 6 cases (13.3%) and malignant 18 cases (40%) compares well with that reported in the literature [11]. Moreover, the surgical margins were negative in 33 cases (73.3%) and positive in 12 cases (26.6%), which is also consistent with that reported in the literature [11]. Although, we aimed surgically for a one cm clear margin, we considered "no tumor on ink" as a negative margin. A watch and see policy was applied to those with a benign PT who had a positive margin, which has been suggested [1,12,13]. Although the literature suggests that a positive margin is the most important predictor of a local recurrence, in our series, only 1 of 12 patients with a positive margin developed a local recurrence, despite no re-excision was performed for all 12 patients with a positive margin [12,13]. In this series, 17 of 21 patients with benign PT had wide local excision and 6 had a positive margin, and despite no re-excision were performed; only one patient developed a local recurrence. Our data supports the safety use of wide local excision for benign PT regardless of the tumor size. It also supports a "watch and see" policy for benign PT with a positive margin. This finding is consistent with the experience of others [1,12-14].

Three of the six malignant PT with a negative margin developed a local recurrence, and none of the 6 patients with positive margin developed a local recurrence, despite our "watch and see" policy for all cases with a positive margin. But we would recommend in the future routine re-excision for all borderline and malignant PT with a positive margin. However, three of the local recurrences had negative margins after their initial wide local excision. Therefore a negative margin does not protect from a local recurrence, and patients with borderline and malignant PT require a life-long surveillance and close follow-up. The overall local recurrence rate in this study was 8.9% (4 of 45 cases), less than that reported by the WHO (21%) [15,16]. The local recurrence rate for benign, borderline and malignant was 4.8%, 0%, and 16.7% compared to the WHO series of 17%, 25% and 27% respectively, despite our malignant PT were larger than 5 cm in 77.8% [15]. On the other hand the incidence of local recurrence among malignant PT following a wide local excision was high 37.5% (3 of 8 patients). This high rate of local recurrence cautions us to perform a wide local excision for malignant PT larger than 5 cm and supports the use of

simple mastectomy; this is in line with the experience of others [17]. None of the three local recurrences had a positive margin. All three local recurrences were salvaged with a simple mastectomy. None of the malignant PT who underwent a simple mastectomy developed a local recurrence, a finding also reported by others [4,16]. Thus, we believe that the best surgical procedure for borderline and malignant PT larger than 5 cm is a simple mastectomy with or without immediate reconstruction [16]. Distant metastasis developed in six patients with malignant PT. Therefore, the rate of metastasis for malignant PT was 33.3% (6 of 18 cases), which is in agreement with that reported in the literature (25% to 40%) [18-21]. There were only two mortality cases among those affected with malignant PT. Therefore the mortality rate was 4.4% for the entire group and 11.1% for the group with malignant PT. This is similar to that reported in the literature (3% to 12%) [21]. However, the reported rates of local failure, distant metastasis and overall survival are very variable [1,18-20], reflecting the retrospective nature of these studies, study period, different histological classification systems used, variable tumor size, and the wide range of surgery performed. Therefore it is difficult to compare our data with these studies. In our study, the type of surgery was determined by the size of the tumor "breast-tumor size ratio", histologic subtype of PT, patient preference and the ability to achieve free surgical margins with acceptable cosmesis. In this series, the majority of benign PT (81%) had a wide local excision, and the majority of borderline PT (66.7%) and malignant PT (55.6%) had a mastectomy.

Based on our data; WLE seems to be an acceptable surgical option for all PT less than 5 cm in size and for benign PT larger than 5 cm. Re-excision is not required for benign PT if clear margins are not achieved; instead a watch and see policy is a safe option [22]. A recurrent benign PT can safely be re-excised provided acceptable cosmesis is achieved. Mastectomy with or without reconstruction is the best option for primary borderline and malignant PT larger than 5 cm in size, and for recurrent borderline and malignant PT. The reported incidence of axillary metastasis is extremely rare [1,4,19,20], therefore, Axillary Lymph Node Dissection (ALND) is not indicated, and none of our patients had an axillary dissection. Several studies do not recommend ALND in patients with PT [1,4,19,20,22].

Moreover, in our series, three malignant PT with a positive margin received radiotherapy. None of our patients received chemotherapy. Firm conclusions on the impact of adjuvant therapies following surgery cannot be drawn from the literature due to the small number of patients studied in various cohorts, therefore, we do not recommend chemotherapy or radiation therapy [1,4,19,20,22]. Our results have to be interpreted with caution, because of the small sample size, short follow up, and the retrospective nature of the study. The small series in our study does not allow proper evaluation of prognostic factors associated with clinical outcome such as local recurrence, distant metastasis and overall survival. But the results of this small study strongly support the surgical value and prognostic significance of the WHO pathological classification of PT into benign, borderline and malignant. This is in line with that reported by others [1,19,20].

Conclusion

Our data suggest that high local control rates can be achieved with WLE in patients with benign PT. However, total mastectomies are recommended for borderline and malignant PTs larger than 5 cm.

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