International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Phyllodes Tumour of the Breast. A Case Series Of 53 Patients in Malaysia

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Abstract

Background: Phyllodes tumour of the breast is a rare entity, accounting for 0.5% of breast neoplasms. It's treatment and prognosis are variable, and still up for debate.

Objective: The purpose of this study is to explore the clinicopathologic features and treatment strategies of patients who underwent surgical treatment of phyllodes tumour at our institution.

Materials and methods: We retrospectively reviewed the medical records of 53 patients who had surgical treatment for phyllodes tumour in Hospital Putrajaya between January 2020 - October 2023.

Results: The mean age was 45.3 (22-80 years). The tumor grades were classified as benign (23 cases, 43.4%), borderline (16 cases, 30.2%) and malignant (14 cases, 26.4%) based on WHO grading system. The mean tumoral size was 112 mm (17-365). Thirty-one (58.5%) patients underwent a local excision of tumor (18 benign and 9 borderline cases) and twenty two patients (41.5%) underwent a mastectomy with or without reconstruction (5 benign, 7 borderline and 14 malignant). 9 of our patients underwent radiotherapy (4 borderline and 5 malignant). The 4 cases of borderline phyllodes had undergone mastectomy and had inadequate margin clearance. Among of our cases of malignant phyllodes, 5 (35.7%) of them had metastatic disease at presentation, and 2 patients progressed to metastases during follow up. Local recurrence developed in 6 patients, (4 malignant, 1 borderline, 1 benign), giving a local recurrence rate of 28.6% for malignant, 6.25% for borderline, and 4.3% for benign respectively. The shortest time to the development of local recurrence in malignant disease was 3 months, further highlighting the aggressiveness of the malignant variant of phyllodes. In our results there was a significant correlation between tumour size and grade.

Conclusion: PT represents a heterogeneous group of tumours with an unpredictable outcome. Histopathological classification is the strongest prognostic factor for prognosis and a larger size at presentation should increase the suspicion of malignancy.

Keywords: phyllodes tumours, breast neoplasm, surgery, Malaysia

Introduction.

Phyllodes tumours (PTs), previously known as cystosarcoma phyllodes, account for 0.5% to 1.0% of all breast tumours and 2.5% of all fibroepithelial tumours [1]. PTs are usually seen in women aged 35 to 55 years, and only a few cases have been reported in men [2, 3].They derive their neoplastic potential from mesenchymal cells and are thus histologically distinguished from adenocarcinoma of the breast [4]. PTs are histologically classified by the World Health Organization (WHO) as benign (35%– 64%), borderline, and malignant (10%– 30%). Malignant PTs tend to recur and metastasize at a higher frequency than the

other forms of PT [2]. Surgical excision with negative surgical margins is the mainstay of treatment and is associated with relatively high disease-free survival and long-term survival rates and a low recurrence rate [5]. Radiation therapy (RT) is often used because PT tends to be locally aggressive [6]. The role of chemotherapy and hormonal therapy has not been established.

Objectives

Given the paucity of data regarding PT in Southeast Asia, the aims of this study were as follows:

1. Review the cases of PT in patients treated at a single tertiary health care centre in Malaysia
2. Describe the patient profile, clinicopathological features, treatment strategies and clinical outcome of patients who underwent surgical treatment of phyllodes tumour at our institution.
3. Compare the characteristics of patients with PT treated at our centre with the data available in the literature

Methodology

This is a single-institution retrospective case series performed at Putrajaya Hospital, a tertiary health care centre in Malaysia. All cases of PT of the breast that underwent surgery at Putrajaya Hospital, from 1 January 2020 to 31 October 2023 were included in this study. Patients of all ages with a histologically proven PT of the breast, and had undergone surgery, were eligible for inclusion. Each patient's hospital medical chart was reviewed for demographic data, clinical data, and pathological findings. Pathology reports were reviewed to obtain data on the histological type and WHO tumour grade. Each patient's treatment was also evaluated (surgery, RT, systemic therapy, combined-modality treatment, or observation).

The data were compiled with IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, NY, USA) using identification numbers. Statistical analysis was performed using SPSS. Descriptive analyses of demographics, treatment modalities, and tumour characteristics were conducted. A Pearson chi-square test was used to investigate the relationship between age and tumour size with histological type of PT.

Results

Patient characteristics

We identified 53 patients in our medical registry who underwent surgical treatment for phyllodes tumor between 1 January 2020 and 31 October 2023. The mean age of the study population was 45.3 years (22-80yo). The mean ages for benign, borderline and malignant PTs were 44.3, 45.5 and 47.3 years, respectively. 84.9% of patients with PT were of the Malay ethnicity. 1.9% of patients were Chinese, followed by Indian and other race groups. Table 1 shows the demographic features of benign, borderline and malignant phyllodes tumour (n=53).

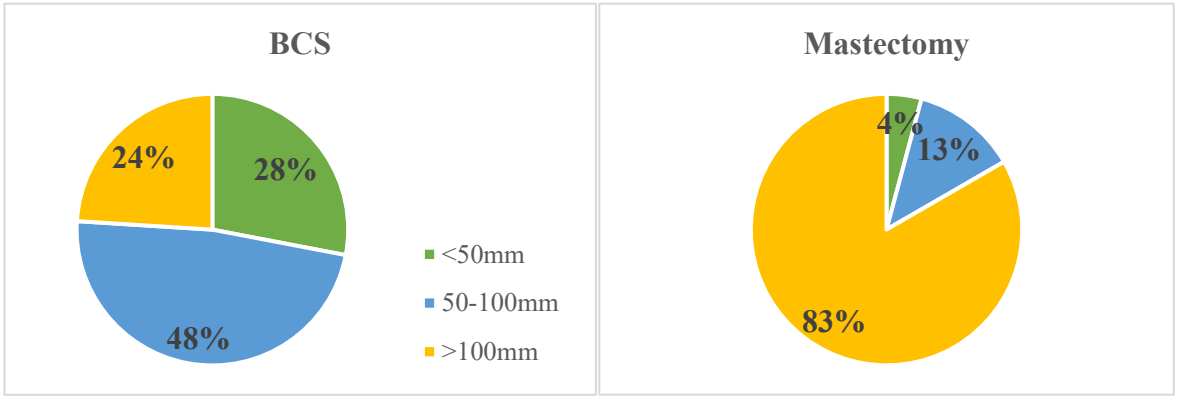
Table 1: Demographic features of benign, borderline and malignant phyllodes tumor (n= 53)

		Benign (n=23)	Borderline (n=16)	Malignant (n=14)
Ethnicity				
	Malay	19 (82.6%)	13 (81.3%)	13 (92.9%)
	Chinese	3 (13%)	2 (12.5%)	1 (7.1%)
	Indian	0 (0.0%)	1 (6.3%)	0 (0.0%)

	Others	1 (4.3%)	0 (0.0%)	0 (0.0%)
Age				
	Range	22-74	26-65	32-80
	Mean	44.3	45.5	47.3

There was no statistically significant correlation between age and histology of phyllodes (p=0.85) in our study. The tumour grades based on WHO grading system were classified as benign (23 cases, 43.4%), borderline (16 cases, 30.2%) and malignant (14 cases, 26.4%). All patients underwent surgery. Thirty-one (58.5%) patients underwent a local excision of tumour (18 benign and 9 borderline cases) and twenty-two patients (41.5%) underwent a mastectomy with or without reconstruction (5 benign, 7 borderline and 14 malignant). The mean tumoral size was 112 mm (17-365). Mastectomy was performed in 76.9% of tumours larger than 100 mm. There was a significant correlation between tumour size and histology (p<0.1)

Figure 1: The relationship between surgical treatment and tumour size



Tumor margins were compromised in 20 cases, of which 5 were malignant PT. In our study, we defined tumor margin compromise as margin that was less than 10mm. we excluded deep and ventral margins, as there margins would have been limited by the underlying pectoralis muscle or the overying skin. 3 of the cases of malignant phyllodes with compromised margins went on to develop local recurrence within 3 months to 1 year. 9 of our patients underwent radiotherapy (4 borderline and 5 malignant). The 4 cases of borderline phyllodes that underwent radiotherapy had undergone mastectomy and had inadequate margin clearance. Among our cases of malignant phyllodes, 5 (35.7%) of them had metastatic disease at presentation, and 2 patients progressed to metastases during follow up. Our mean follow up was 14.2 months. 47 patients (88.9%) were stable at last follow up and had no disease recurrence. Local recurrence developed in 6 patients, (4 malignant, 1 borderline and 1 benign), giving a local recurrence rate of 28.6% for malignant, 6.25% for borderline, and 4.3% for benign respectively. The shortest time to the development of local recurrence in malignant disease was 3 months, further highlighting the aggressiveness of the malignant variant of phyllodes. The case of benign phyllodes, developed a local chest wall recurrence post mastectomy that revealed a histology of borderline phyllodes. The patient then went on to develop spinal metastasis.

Table 2: Type of surgery, margins, development of local recurrence and metastasis during follow up period

		Benign (n=23)	Borderline (n=16)	Malignant (n=14)
Type of Surgery	Local excision	18	9	0
	Mastectomy	5	7	14
Tumor Size	<50mm	6	1	1
	50-100mm	6	8	1
	>100	9	5	12
Surgical Clearance	<10mm	8	7	5
	≥10mm	12	6	9
	unknown	3	3	0
Radiotherapy	Yes	0	4	5
	No	23	12	10
Local Recurrence	Yes	1	1	4
	No	22	15	10
Metastasis	Yes	1	1	5
	No	22	15	9

Discussion

PT accounts for 0.5% to 1.0% of all breast tumours and 2.5% of all fibroepithelial tumours [1]. It is composed of epithelial and mesenchymal elements, the latter giving it its neoplastic features [4]. The WHO identified three types of PT based on its histologic characteristics: benign, borderline, and malignant [7]. These types help to predict the likelihood of developing local recurrence, metastatic disease, or both. Of the 53 cases of phyllodes tumours in our study, Most of the tumours (43.4%) were benign, similar to the 35% to 64% rate of benign disease cited in the literature [2]. Our finding that 26.4% of patients had malignant disease is consistent with previous studies, which showed that 10% to 30% of patients with PT have a malignant course [2]. These have a higher chance of recurrence and metastasis [2].

PT occurs most frequently in women aged 35 to 55 years and presents as a well- circumscribed, smooth, firm, and painless mass [2]. The mean age at presentation of our cases was 45.3 years with no significant difference in mean age between the benign, borderline or malignant categories.

Mammography and ultrasound appearances are non-specific, and it is often difficult to differentiate PT from fibroadenoma on sonography or mammography. It is also not possible to distinguish between benign and malignant PTs based on sonographic or mammographic findings. Magnetic Resonance Imaging may be used to delineate the full tumour extent and potential satellite lesions before surgical excision.

Surgical treatment is generally accepted as the most important and primary therapy for phyllodes tumours, regardless of its histological type. Wide surgical excision with a margin of more than 1 cm even when pathologic features suggest the tumour is benign is currently recommended. Mastectomy is necessary only when tumour cannot be removed with adequate clearance.

Mastectomy and BCS offer comparable survival benefits [10]. 58.5% patients underwent BCS whilst 41.5% of our patients underwent mastectomy with or without reconstruction. This higher margin of mastectomy compared to wide local excision could be attributed to the larger tumour size at presentation. We had a mean tumoral size of 109mm (28mm-220mm) in comparison with literature that described mean tumoral sizes between 50 to 90mm [11].

In our case series, comparable to other studies, malignant tumours (mean size= 15.5cm) had a larger tumour size compared to its benign and borderline counterparts. However, the benign tumour sizes in our case series (mean = 8.9cm) is larger compared to those described in other studies [11]. These values not only reflect the rapid growth and aggressiveness of malignant and borderline tumours, but it also highlights the issue of delayed presentation of patients to healthcare centres in our setting, thus leading to larger tumours at initial presentation.

The likelihood of local recurrence and distant metastasis in patients with PT is mainly determined by the histotype of the tumour and the margins after resection [12]. In two studies, all patients with recurrence of PT had positive surgical margins [5, 13]. Thus, negative margins might improve long-term survival and disease-free survival and reduce recurrence [5].

Our findings agree with this data. In 4 out of the 6 cases of local recurrence, (66.7%) patients in whom a local recurrence occurred, the width of the resection margin had been less than 10 mm. This elucidates the importance of having an adequate resection margin during initial surgery. Thus, preoperative diagnosis is then important for good local control. Wide re-excision should be considered when the margins are involved microscopically.

Metastasis in PT usually spread hematogenously to the lungs, pleura, or bone. Because axillary lymph node metastasis occurs in <1% of patients with PT, axillary lymph node dissection is not routinely performed [2]. In literature, the incidence of metastatic spread of malignant phyllodes tumours varies from 25 to 40%[8] which is in the range of our data showing a rate of 35.7% in this patient group.

The role of adjuvant RT remains debatable despite its common use in patients with positive or close resection margins. This is due to the absence of large prospective trials to give convincing evidence of a survival benefit. However, RT needs to be considered to boost the effect of surgery and improve local disease control [5, 6]. A meta-analysis of eight studies showed a significant decrease in the risk of local recurrence in patients with borderline and malignant PTs who received adjuvant RT after BCS (hazard ratio [HR], 0.31; 95%CI, 0.10–0.72), but there was no difference in the combined HR for local recurrence in the total mastectomy group with versus without RT (HR, 0.68; 95% CI, 0.28–1.64). However, overall survival and disease-free survival were not altered by adjuvant RT in either group [14].

Nine patients in our population received adjuvant RT. All these patients were given radiotherapy due to inadequate margin clearance of <1cm. These patients had either borderline or malignant phyllodes. None of the patients who underwent radiotherapy developed local recurrence.

There is no definitive evidence regarding the role of chemotherapy, and the indications for chemotherapy, and the best treatment regimen has yet to be published. Mostly are retrospective studies and case series that have produced conflicting reports concerning the benefit of chemotherapy [15, 16]. Doxorubicin and ifosfamide based chemotherapies have shown some efficacy in women with metastatic spread of phyllodes tumours [16].

In our study population, only 2 patients underwent palliative anthracycline-based chemotherapy for metastatic malignant phyllodes, and they eventually succumbed to the disease.

Limitations

As noted above, this study is limited by the small number of patients included in the analysis. This limitation is caused by the rarity of PT, and the inclusion of only one hospital centre. The data extraction relied solely on a review of electronic medical records. Another limitation of this study is the short follow up period. The reason for this could be because Hospital Putrajaya is a tertiary referral centre and patients

who come from other parts of the country find it inconvenient to return for long- term assessment and follow-up, and hence they choose to continue their follow up in the district hospitals.
This short follow up period may introduce a bias causing an underestimation of the incidence of recurrence or metastasis. A long follow up period would help determine a more accurate prognosis and local recurrence rates and determine significant correlations between other clinical or pathological parameters. Nevertheless, this remains the first cohort of patients with PT described in Hospital Putrajaya and one of few described in Malaysia, and it provides helpful insight into the epidemiology, treatment modalities being used, and prognosis of PT in this geographical region.

Conclusion.

PT represents a heterogeneous group of tumors sharing the same macroscopic features with an unpredictable out- come. Surgery remains the cornerstone of treatment consisting of wide local excision with adequate margins of healthy surrounding breast tissue at initial therapy. This study has provided a few valuable insights into phyllodes tumours in the Malaysian setting. Despite the small sample size of our study population, it remains mostly consistent with the available literature regarding the epidemiology, tumour characteristics, and treatment course of PT. In our setting, the issue of delayed presentation leading to large breast masses, and metastases in malignant tumours is very concerning. Issues with patient education and awareness need to be addressed to ensure early and prompt management.

Consent and ethical approval

As per standard guideline, participant consent and ethical approval have been collected and preserved by the authors.

Competing interests

Authors have declared that no competing interests exist.

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