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Radiopathological characteristics and outcomes of phyllodes tumor of the breast in Malaysian women

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Abstract

Phyllodes tumor or cystosarcoma phyllodes is a rare fibroepithelial neoplasm which arises from the periductal stroma of the breast. They are classified as benign, borderline, and malignant based on the histologic features. However, all phyllodes tumor (PT) subtypes are regarded as having malignant potential and correct diagnosis is important for surgical management and optimal care. This study is a retrospective review of 76 women diagnosed as PT with highlights on the imaging characteristics, pathology, and surgical treatment over a 7-year period in a tertiary medical center of urban population in Malaysia. There were 45 benign, 16 borderline, and 15 malignant PT. The median age for benign PT was 43, borderline 48.5, and malignant 42 years. The Malay ethnic group constitute 52.6% of cases, with 27.6% and 18.4% in Chinese and Indian ethnic groups, respectively. On mammograms, most benign (64.3%) and 33.3% of malignant PT showed high-density lesions. Calcifications were only seen in 2 benign PT. On ultrasound, 86% of benign PT was well-circumscribed whilst 50.0% of malignant PT had irregular outline. Cystic spaces were seen in 40.0% of malignant and 9.5% of benign PT. 80% of malignant PT lesions were heterogenous. Malignant PT demonstrates tumor heterogeneity, cystic spaces, and posterior acoustic enhancement on ultrasound. Half of malignant PT showed regular borders on ultrasound and appear well circumscribed on mammogram. A total of 46 patients had wide local excision or excision biopsy whilst 30 underwent mastectomy as primary treatment. The majority of the borderline and malignant PTs in our study (75.0% and 85.7% respectively) and only 5 out of the 43 (11.6%) benign PT underwent mastectomy. There were 2 tumor recurrence in the benign PT group and 1 case in the borderline and malignant group respectively.

Abbreviations: ACR = American College of Radiology, BIRADS = Breast Imaging Reporting and Data System, CC = cranio-caudal, DWI = diffusion weighted imaging, FNAC = fine needle aspiration cytology, MHz = megahertz, MLO = mediolateral oblique, MRI = magnetic resonance imaging, PT = phyllodes tumor, STIR = Short Tau Inversion Recovery, SWE = shearwave elastography, T1FS = T1 weighted fat saturation sequence, T1W = T1 weighted sequence, T2W = T1 weighted sequence, US = ultrasound, WHO = World Health Organization, WLE = wide local excision.

Keywords: histopathology, MRI, phyllodes tumor, radiology features, surgical management

1. Introduction

Phyllodes tumor (PT) of the breast is a rare fibroepithelial neoplasm representing <1% of all mammary tumors.[1–3] The name phyllodes originates from Latin (phyllodium) and Greek (phullōdēs) which mean leaf-like or flattened leafstalk. Histologically, it is characterized by large leaf-like (phyllodes) projections with high degree of increased stromal proliferation and cellularity as compared to fibroadenoma.[3] Due to its rarity, there has been considerable debate regarding its nomenclature, histopathologic diagnosis, radiological presentation, and treatment options and recurrence.

In 1982, World Health Organization (WHO) classified phyllodes tumor into benign, borderline, and malignant based on a combination of several histologic features, including stromal cellularity, nuclear atypia, mitotic activity, stromal overgrowth, and tumor margin.[2] However, the diagnosis of PTs based on the integration of morphology remained challenging, particularly in the distinction of PTs from fibroadenoma as there are no defined criteria or clear cutoffs for individual histologic parameters.

Surgery has been the mainstay of treatment for all subtypes of PTs, however the extent of resection, that is wide local excision (WLE) or mastectomy and the role of adjuvant radiotherapy and chemotherapy for PT are still debatable.[4] Although most PTs behave in a benign fashion, the risk of recurrence is 4.7% to 30% for benign and 30% to 65% for borderline and malignant PT. Distant metastasis occurs in up to 22% of malignant PTs. The histologic grading of PT generally correlates with prognosis.[3]

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To date, there is limited clinical data with regard to imaging and pathological correlation of PT in the multiethnic Malaysian population. Given the rarity of this disease, our aim is to describe the radiological, pathological and clinical outcome of PT in multiethnic Malaysian population.

2. Material and methods

This is a retrospective clinical study of all women with histopathologically confirmed phyllodes tumors (PTs) who were diagnosed and presented at the University Malaya Medical Centre (UMMC) over a period of 7 years (2008–2015).

The pathology registry database identified 76 confirmed cases of PTs. Patients' medical records were retrieved and analyzed for demographic data, radiological features, presurgical diagnosis, types of surgical treatment, and follow-up records.

Written inform consent was not required as this was a retrospective observational study. All clinical data were used in anonymized form and we confirmed that all methods were performed in accordance to the institution guidelines and regulations. Ethical approval was granted by the Medical Ethics Committee of University Malaya (MEC No 2017123-4838).

2.1. Histopathological classification

All the archived histopathological slides were reviewed and classified by a consultant pathologist blinded to the clinical outcome. PTs was subdivided into benign, borderline or malignant subtypes based on the WHO "Blue Book" on Classification of Tumours of the Breast.[5]

Histological features such as mitotic activity of tumor cells per 10 high power field, degree of cellular atypia and the presence/absence of stromal overgrowth and necrosis were documented. Cellular atypia was arbitrarily divided into absent, mild, moderate or marked based on the degree of nuclear pleomorphism. Stromal overgrowth was defined as the presence of only stroma in a single 40× magnification field.

2.2. Radiological assessment

Radiological images were available in picture archive communication system (PACS) from 2010 onward. Mammogram images with ultrasound (US) correlations were available for 23 patients. US images were available for 36 patients and 3 patients had magnetic resonance imaging (MRI) images. All the images were reviewed in consensus by 2 breast radiologists (SH and MT, with 4- and 6-year experience, respectively). Both were blinded to the pathology and clinical outcomes. Only demographic data were included in the study for PT patients without corresponding radiology images.

Digital mammography was performed using General Electric (Senographe Essential, Cedex-France) prior to July 2014 and Selenia Dimension (Hologic, Bedford, MA) after July 2014. Standard imaging acquisition consists of bilateral cranio-caudal (CC) and mediolateral oblique views (MLO). In selected cases, additional spot compression and magnification views were available.

All US scans were performed using diagnostic B-mode grayscale and color, medical grade US system (Philips iU22; Philips Healthcare, Bothell, WA) with a high frequency (i.e., 12.5 MHz) linear transducer probe. Spot images were captured in transverse, orthogonal and colour Doppler imaging.

The morphology of the breast lesions on mammograms and US were qualitatively analyzed and characterised according to the American College of Radiology's Breast Imaging Reporting and Data (ACR BI-RADS) 5th Edition 2014 classification system.[6] Shape, margin, density, calcification, and architectural distortion were documented for mammogram. The size, shape, echogenicity, orientation, margin, and posterior acoustic features of the lesion were documented for US. Vascular patterns of PT were assessed by the presence of penetrating vessels, peripheral vascularity, or the absence of vessel similar to that described by Ibrahim et al.[7]

Breast MRI were performed using General Electric Signa HDx 3.0T MR scanner (GE Medical Systems, Waukesha, WI). Standard breast MRI protocols were used. The sequences include Axial T1 FS, T2, STIR, and 6 dynamic postcontrast sequences with its corresponding subtracted images. As per routine and in accordance with ACR BIRADS 5th edition classification system, the shape, margin, enhancement characteristic, and kinetic curve analysis of the PT were evaluated on MRI.

Ultrasound-guided core biopsy was performed by breast radiologists using 14-gauge core biopsy needle. A minimum of 3 to 5 core biopsy specimens were obtained for each lesion. Fine needle aspiration cytology (FNAC) was performed for palpable breast lesions by breast surgeons in the breast clinic.

2.3. Data availability

The datasets generated during and analyzed during the current study are available from the corresponding author on reasonable request.

2.4. Statistical analysis

Statistical analysis was performed using SPSS software version 20 for Mac (SPSS Inc., Chicago, IL) with the Chi-squared test.

3. Results

A total of 76 patients with histological diagnosis of phyllodes tumor were identified within this 7-year period and were included in this retrospective analysis. There were 45 benign, 16 borderline, and 15 malignant PT (Fig. 1)

PT was more prevalent in the Malay compared to Chinese or Indian ethnic groups (40, 21, and 14 cases, respectively) (Chi-square 42, $P < .001$). 7 of the 15 malignant PT (46.7%) and 27 of the 45 benign PT (60.0%) were found in the Malay ethnic group (Table 1). The results were statistically significant in all the PT subtypes (benign, borderline and malignant) (Chi-squared 18.7, $P < .001$)

The median age of PT was 45 years (range, 12 –73) (Table 1). No significant difference was seen in the median age for benign, borderline, and malignant PT (Chi-squared 16.3, $P = .177$). The mean age for benign PT was 41.8 years (12–67 years) and 40.0 years (24–73 years) for malignant PT. Borderline PTs however showed a higher mean age of 51.1years (34–72 years) (Chi-squared 16.3, $P = .177$).

Of the available clinical history (53 patients), 4 were diagnosed from screening population with a screening duration of 1.5, 3.0, 4.0, and 5.0 years before the PT were diagnosed (Fig. 1). Around 49 patients presented with a lump (31 with progressively enlarging lump of 2 months to 2-year duration, 10 with painless, and 8 with painful lumps).

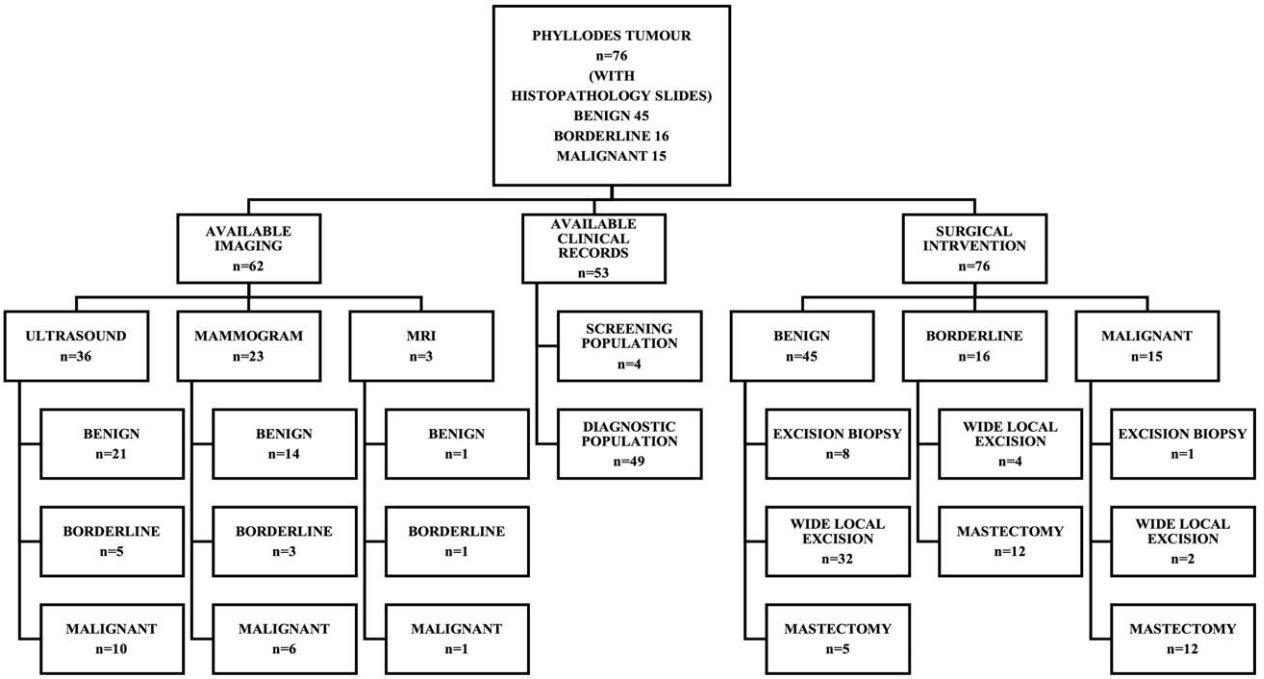

Figure 1. Flowchart of key findings amongst patients included in the study.

3.1. Radiological findings

Around 45 patients had information on laterality. PTs were found in the left in 48.9% (n=22) and in the right in 51.1% (n=23) of cases.

Tumor size was categorized as below 5 cm, 5 to 10 cm and above 10 cm. About 50.0% (n=5) of malignant, 40% (n=2) of borderline and 14.3% (n=3) of benign PT were >10 cm. Most benign PT measured <5 cm (61.9%) (Not statistically significant, Chi-square 5.7, $P=.22$) (Table 2).

The mammographic density of the 23 patients were characterized in accordance to the ACR BI-RADS 5th Edition 2014 classification system. Around 4 had mammographic density B. The other 19 (82.6%) had mammographic density C or D. High-density appearance with well-circumscribed margin was seen in 56.5% (n=13) of cases. Most benign PT (64.3%, n=9) and 33.3% (n=2) of malignant PT were high-density lesions. Macro and microcalcification were seen in 2 benign PT (Fig. 2).

Of the 36 patients with US, posterior acoustic enhancement was seen in most cases (86.1%, n=31). No particular vascularity pattern was observed in any of the PT subtype on colour Doppler. The majority of benign PTs (86.1%, n=18) have well-circumscribed margin. Irregular margin was seen in 14.3% (n=3) benign and 50.0% (n=5) malignant PT. 40.0% (n=4) of the malignant, 40.0% (n=2) of the borderline and 9.5% (n=2) of benign PT demonstrated presence of intratumoral cystic spaces within the solid tumor on US. However, these results were not statistically significant (Chi-squared test 4.7, $P=.10$). Most malignant PT (80%) (n=8) showed a heterogeneous echotexture (Fig. 3).

3.2. Chi-squared test did not show significant difference in any of the mammographic and ultrasound findings in all 3 PT subgroups

There were 1 benign, 1 borderline, and 1 malignant PT images available on MRI (Table 2). Benign PT was seen as a small well-

Table 1

Characteristics of the patients according to PT subtypes.

	Benign	Borderline	Malignant	Total	Chi-squared test (*P* value)
No of PT	45	16	15	76	
Median Age (Standard deviation)	43.0 (15)	48.5 (12)	42.0 (14)	45	16.3 (0.18)
Ethnicity (%)					18.7 (0.001)*
Malay	27 (60.0)	6 (37.5)	7 (46.7)	40 (52.6)	
Chinese	9 (20.0)	8 (50.0)	4 (26.7)	21 (27.6)	
Indian	9 (20.0)	1 (6.3)	4 (26.7)	14 (18.4)	
Others		1 (6.3)		1 (1.3)	
Laterality (%)					0.8 (0.69)
Right	12 (52.2)	4 (45.5)	7 (58.3)	23 (51.1)	
Left	11 (47.8)	6 (54.5)	5 (41.7)	22 (48.9)	
	23	10	12	45	

PT=phyllodes tumor.
* The group others was excluded from this analysis.

Table 2

Imaging findings and characteristics on mammogram or ultrasound according to PT subtype.

	Benign	Borderline	Malignant	Chi-squared test (*P* value)
Mammogram n = 23	14	3	6	
Density				
Isodense	5	1	4	1.8 (*P* = .41)
High density	9	2	2	
Lucent halo				
Present	12	3	3	4.1 (*P* = .13)
Absent	2	0	3	
Calcifications				
Present	2	0	0	1.4 (*P* = .50)
Absent	12	3	6	
Margin				
Well-defined	12	3	3	4.1 (*P* = .13)
Obscured	2	0	3	
Ultrasound n = 36	21	5	10	
Size				
<5 cm	13 (61.9)	3 (60.0)	4 (40.0)	5.7 (*P* = .22)
5–10 cm	5 (23.8)	0	1 (10.0)	
>10 cm	3 (14.3)	2 (40.0)	5 (50.0)	
Outline				
Well	18	4	5	4.7 (*P* = .10)
Irregular	3	1	5	
Echogenicity				
Hypoechoic	7	3	2	2.4 (*P* = .30)
Heterogeneous	14	2	8	
Cystic spaces				
Present	2	2	4	4.7 (*P* = .10)
Absent	19	3	6	
Posterior enhancement				
Present	18	5	8	0.8 (*P* = .67)
Absent	3	0	1	

PT = phyllodes tumor.

circumscribed lobulated predominantly isointense mass on T1W and STIR, hypointense on T2W and demonstrates progressive enhancement on the postcontrast sequences consistent with type I curve (Fig. 4). No restricted diffusion or nonenhancing septae seen within. Borderline PT showed a predominantly hypointense signal on T1W, hyperintense on T2W, restricted diffusion on DWI, and progressive enhancement followed by plateau in keeping with type II curve on the postcontrast sequences (Fig. 4). Malignant PT showed hyperintense mass on T1W and T2W sequences with rapid contrast uptake with washout pattern, in keeping with type III curve.

3.3. Diagnosis

Of the 76 patients with PT, 56 had initial core needle biopsy, 14 had initial FNAC. Around 6 patients underwent surgery without presurgical histological diagnosis. Of these 6 patients, 4 had excision biopsy and 2 had mastectomy, for very large ulcerated and bleeding tumors on initial hospital presentation.

Of the 56 patients who underwent core needle biopsy, 35 (62.5%) had PT diagnosed from the initial core biopsy. Of the remainder 21 patients (37.5%), 11 had histopathological diagnoses of fibroadenoma, 2 with fibrocystic disease, 1 with ductal hyperplasia, 1 benign spindle lesion, 1 sarcoma with chondroid differentiation, and 5 "no malignancy." Of the 5 "no malignancy," 4 were benign PT on excision biopsy and 1 was high grade sarcoma on excision biopsy and malignant PT on mastectomy.

In the 35 patients with proven PT on initial core biopsy, there were a total of 11 benign, 4 borderline, and 4 malignant PT. The rest of the PTs were not graded on core biopsy. Of the 11 benign PTs, there was a 27.3% upgrade, in which 1 had a final (postsurgical) histopathological diagnosis of borderline PT and 2 of malignant PT. The rest had similar diagnosis at core biopsy and in the final surgical histopathology.

Of the 14 FNAC only 2 (14.2%) had an initial diagnosis of PT.

3.4. Histopathology examination

For histopathological classification, benign tumors have low mitotic activity and mild cellular atypia whilst malignant tumors generally exhibit higher mitotic activity (> 5 mitoses per 10 high power field) and moderate to marked cellular atypia. Stromal overgrowth (Chi-square = 39, $P < .00001$) and tumor necrosis (Chi-square = 33.25, $P < .00001$) were commoner in higher grade tumors (borderline and malignant). As can be seen in Table 3 and Figure 5, the borderline subgroup tends to have features that straddle between the benign and malignant categories.

3.5. Primary treatment, local recurrence and distant metastasis

Table 4 summarizes the surgical management and outcome of patients according to PT subtypes. A total of 46 patients had WLE or excision biopsy whilst 30 underwent mastectomy as primary treatment.

Of the 15 malignant PT, 12 underwent simple mastectomy, 2 had WLE, and 1 excision biopsy. One of the WLE patients developed recurrence 5 years later despite a clear surgical margin.

Of the 45 benign PT, 32 had WLE, 8 excision biopsy, and 5 simple mastectomy. Two of those who underwent excision biopsies developed recurrence.

There was one recurrence in a borderline PT patient who had involved surgical margins on mastectomy.

4. Discussion

In our study, PT was found more in the Malay ethnic group which is in contrast to breast cancer occurrence which was more prevalent in the Chinese ethnic group in Malaysia.[8] Our study was conducted in a tertiary referral centre which is located in an urban mainly Chinese neighborhood. Teh et al[9] demonstrated that the majority of patients that presented to the breast unit in this center were of Chinese ethnicity. Their paper also demonstrated that the incidence of breast cancer was higher in the Chinese population in Malaysia. Our retrospective study was conducted based on a similar cohort of patients which attended UMMC between 2008 and 2015.

Karim et al[10] showed that 31% of the PT cases in Sydney, Australia were women of Asian origin. Several other studies also

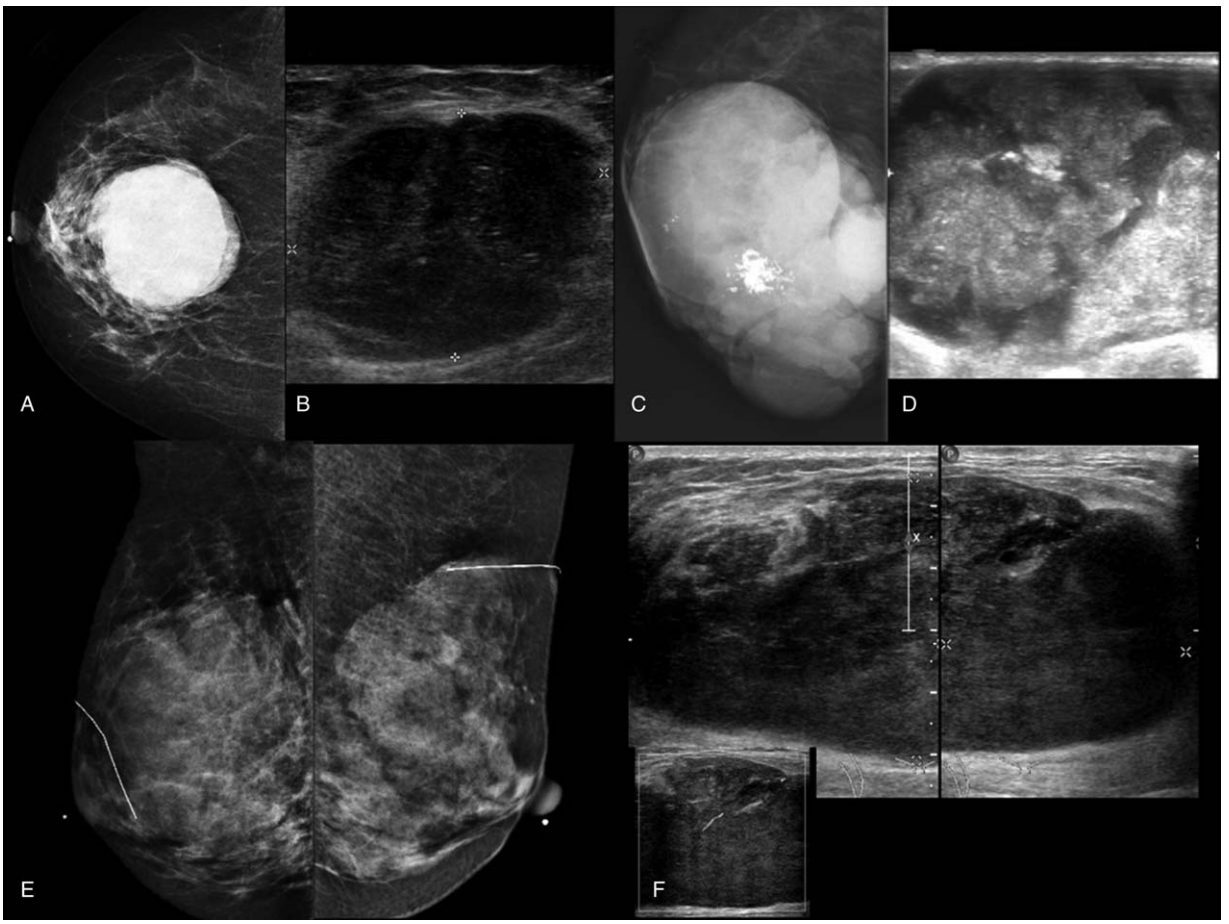

Figure 2. (A) Right mammogram CC view in a patient with benign PT demonstrating a well-circumscribed high-density mass with surrounding lucent halo. (B) Corresponding ultrasound showing a well-defined homogenous hypoechoic lesion. (C) Right mammogram in MLO view in a patient with benign PT showing a high-density lesion with coarse macrocalcifications within. (D) The calcifications within the lesion was also visualised on ultrasound. (E) Mammogram of both breasts of a malignant PT in MLO view demonstrating asymmetric breast density with an ill-defined equal density lesion in the right breast that is not very well appreciated on mammogram. (F) Ultrasound of the right breast revealed a large hypoechoic lesion with irregular outline and internal vascularity in the retroareolar region. MLO = mediolateral oblique, PT = phyllodes tumor.

showed that there were higher incidence of PT among a certain ethnic group compared to others in their region, namely among the African American and the Hispanics in the United States.[1,11]

In the current literature, PTs have been known to occur in females aged 35 to 55 years, which was typically 10 to 20 years older than peak incidence of fibroadenoma.[12–14] Our study also showed an older age profile, that is, median age of 45 years. Our study showed no significant difference in the mean age of patients with malignant and benign PT, that is, 40 versus 41.8 years, respectively, as previously reported.[11] However, previous studies have reported more frequent occurrence of malignant PT in older patients with mean age of 45 to 54.[1,15] In contrast, we found slightly higher age group presenting with borderline PT (mean age of 51.1 years) compared to benign and malignant as seen in another study.[16]

The tumor was almost equally distributed in the right and left breast in all the subtypes. Similar pattern of equal distribution was noted in several other studies.[4,17,18] Two studies however, described a left dominance pattern of 71% and 58%, respectively.[1,16] Clinical data on menarche, menopause, hormone history, or pregnancies were sparse. However, a local study by Yen-Fa et al[19] showed that pregnancy status, breast feeding history, hormonal contraception history, and family history of breast cancer or laterality of tumor were not significantly different between the benign, borderline and malignant PTs.

In our study, 50.0% (n = 5) of malignant lesions, 40.0% (n = 2) of the borderline and 14.3% (n = 3) of benign lesions were larger than 10 cm. The higher proportion between the PT subtypes could be attributed to the rapid growth seen particularly in malignant and borderline PT.[19] Previous studies showed no significant relationship between PT size and histopathological subgroups.[10,20]

In most studies done in the West, the mean size of tumor was around 2.3 to 7.7 cm.[17,20,21] In Malaysia, low breast health literacy and a tendency to seek alternative treatments before allopathic medicine has been reported.[22] This may be a factor for delay in hospital presentation, leading to larger tumor lesions at presentation.

Majority of the borderline and malignant PTs in our study (75.0% and 85.7%, respectively) and only 5 out of the 43 (11.6%) benign PT underwent mastectomy. Up to the end of the 1970s, mastectomy was the standard surgical treatment for all PT, irrespective of histological type or size.[23] However, since then, a more conservative approach to the management has been adopted by many, one of the reasons being that the tumor is

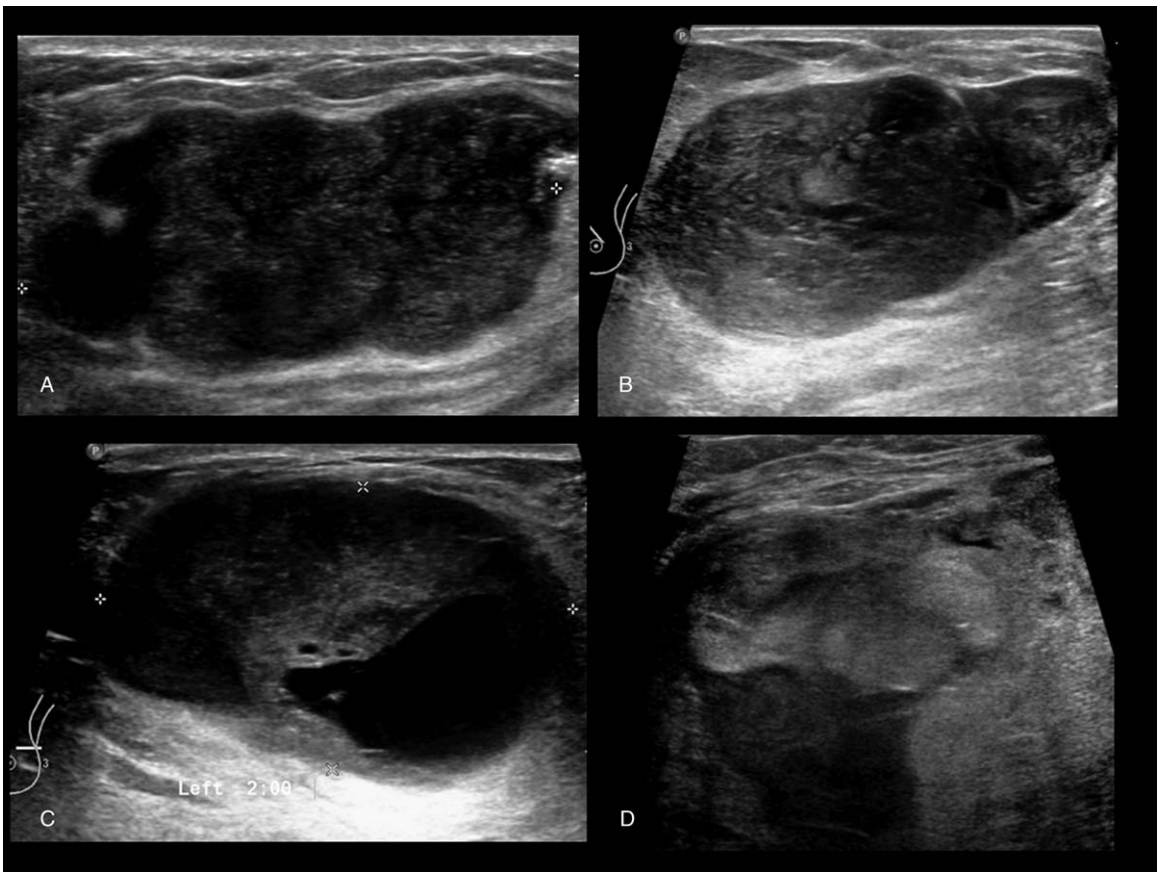

Figure 3. Ultrasound images showing (A) benign PT with lobulated margin (B) Malignant PT with well-defined border and posterior acoustic enhancement. Malignant PT with (C) cystic spaces, (D) heterogeneous internal echo. PT = phyllodes tumor.

rarely multifocal. For tumors <10 cm in size, WLE with a minimal safe tissue margin between 1 and 2 cm is usually regarded as adequate. For tumors larger than 10 cm where the tumor-to-breast ratio is compromised, mastectomy, and breast reconstructive surgery remains the preferred option even in benign PT.[23–26] Axillary nodal dissection is not recommended since malignant PT undergo haematogenous spread and the rate of lymph node metastases is very low.[3,15,20,27,28]

Regardless of their histology, all PTs can recur; the risk of local recurrence is low in benign PT and higher in malignant PT.[19,28,29] One of the risk factors affecting local recurrence in PT is involvement of surgical margins.[2,19,20] Total of 4 out of the 5 patients in our study who developed recurrence were patients who underwent breast conserving surgery. 3 of them had either benign or borderline PT. In our study, one patient had involved margins, one patient had clear margin, while information on surgical margins could not be traced for the other 3 cases.

The role of adjuvant radiotherapy is a matter of debate in many studies.[2,29] Currently, the indication for radiotherapy should be limited to patients with malignant tumors and positive surgical margins when surgical radicalization cannot be performed. The role of adjuvant chemotherapy is even more questionable and not indicated except for metastatic PT.[29]

In our series, the PT showed a high-density appearance on mammography which was characteristic in 56.5% (n = 13) of all cases. The lesions were well-circumscribed with surrounding lucent halo. However, only 2 out of 6 malignant PT appeared as high-density lesion, the rest were isodense or were not well-appreciated due to dense fibroglandular breast parenchyma on mammograms. Studies by Tan et al and Chao et al also documented the presence of lucent halo around the round, well-defined, lobulated, and high-density masses.[30,31] A similar mixed representation of the margins was seen by Blanco in his study where 7 lesions had well-defined margins of which only 1 was malignant.[32] This is also consistent with Damak et al's findings who reported that all the 15 malignant PTs in106 patients showed irregular margins compared to the borderline and benign PTs.[3,30] We found the presence of coarse macro-calcifications within one high density lesion which corresponded histologically to a benign PT. Calcification is seldom present in benign breast lesions,[31,33] in a study comparing sonographic phyllodes features versus fibroadenoma, 3.9% of fibroadenomas in the series displayed microcalcification and even less was seen in PT which was only 1.9%.[31] A higher number of calcifications was seen in the study by Umpleby et al,[34] where 3 out of his 14 cases (21.4%) of PT had coarse calcifications.

Previous studies did not show any reliable sonographic criteria for differentiation between benign and malignant PT.[13,31,32,34,35] In our study, there was presence of intratumoral cystic components in the borderline (40.0%, n = 2) and malignant (40.0%, n = 4) however is this was not statistically significant (Chi-square = 4.7, $P < .10$). Jalaguier-Coudray et al and Wiratkapun et al in their papers reported that in ultrasound, present of internal cystic spaces or round cysts in lesions that appear like fibroadenoma is highly suggestive of phyllodes tumors.[36,37] A previous study has also reported a high percentage of cystic

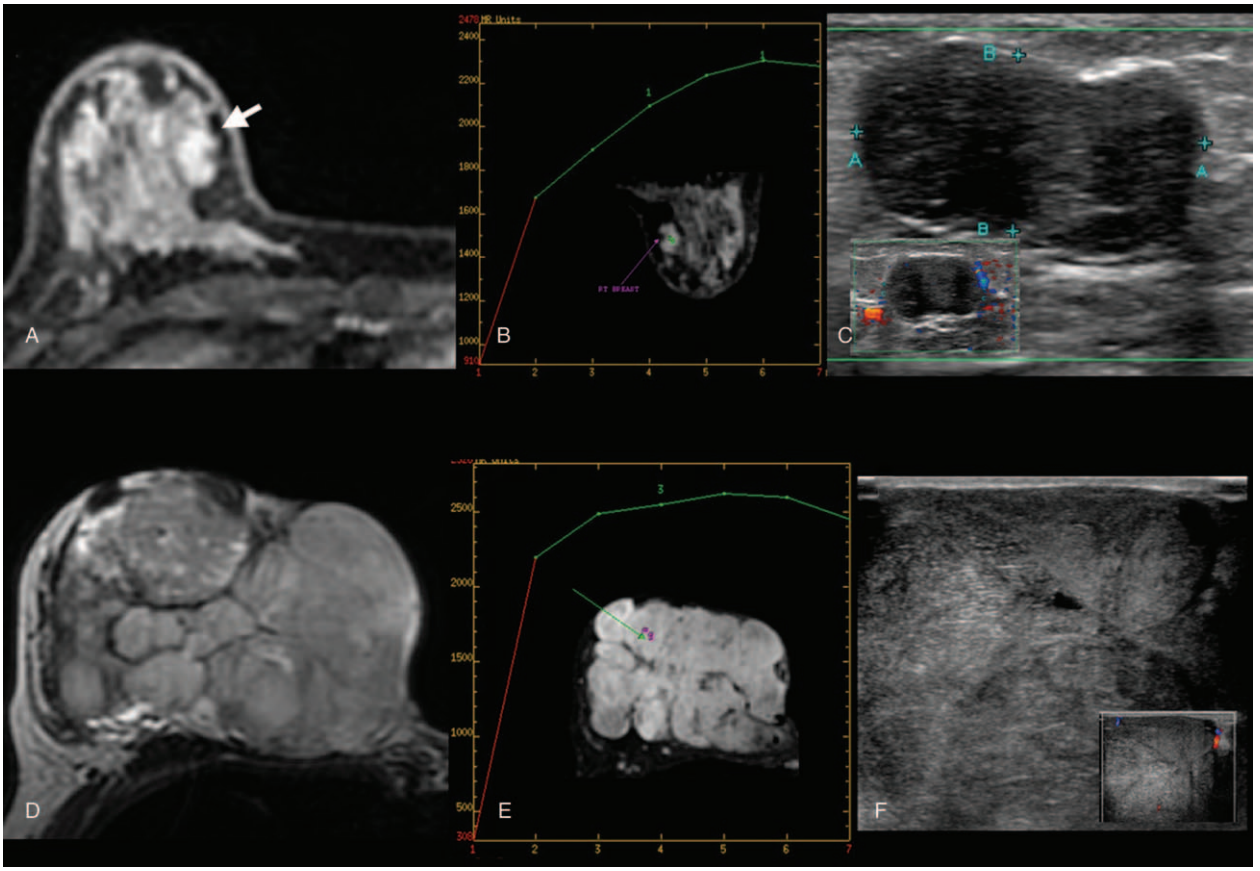

Figure 4. (A) Contrast-enhanced MRI image at 5-minute, shows persistent enhancement of a benign PT in the lower inner quadrant of the right breast with nonenhancing internal septae (B) The kinetic curve demonstrates continuous enhancement (Type 1) in keeping with benign lesion. (C) Corresponding ultrasound images showing a well-defined hypoechoic lesion with perilesional vascularity. (D) Axial T2W MR images of a borderline PT showing a large heterogeneously enhancing mass with internal septae, fat and cystic components occupying the entire right breast. (E) The kinetic curve demonstrates early enhancement that plateau at the later stages in keeping with type 2 curve. (F) Corresponding ultrasound images showing heterogeneous lesion with cystic component and no significant internal vascularity. PT = phyllodes tumor.

Table 3

Histopathological features according to mitotic activity of tumor cells per 10 high power field, the degree of cellular atypia, presence or absence of stromal overgrowth and necrosis.

	Benign (n = 45)		Borderline (n = 16)		Malignant (n = 15)		Chi-squared test (*P* value)
Mitoses (per 10 high power fields)							
0–2	40		2		0		
3–5	2		6		0		
>5	3		8		15		
Cellular atypia	Mild	44	Mild	6	Mild	0	
	Moderate	0	Moderate	8	Moderate	9	
	Marked	0	Marked	2	Marked	8	
	Absent	1	Absent	0	Absent	0	
Stromal overgrowth							39 ($P < .00001$)
Present	2		7		13		
Absent	43		9		2		
Tumour necrosis							33.25 ($P < .00001$)
Present	1		2		10		
Absent	44		14		5		

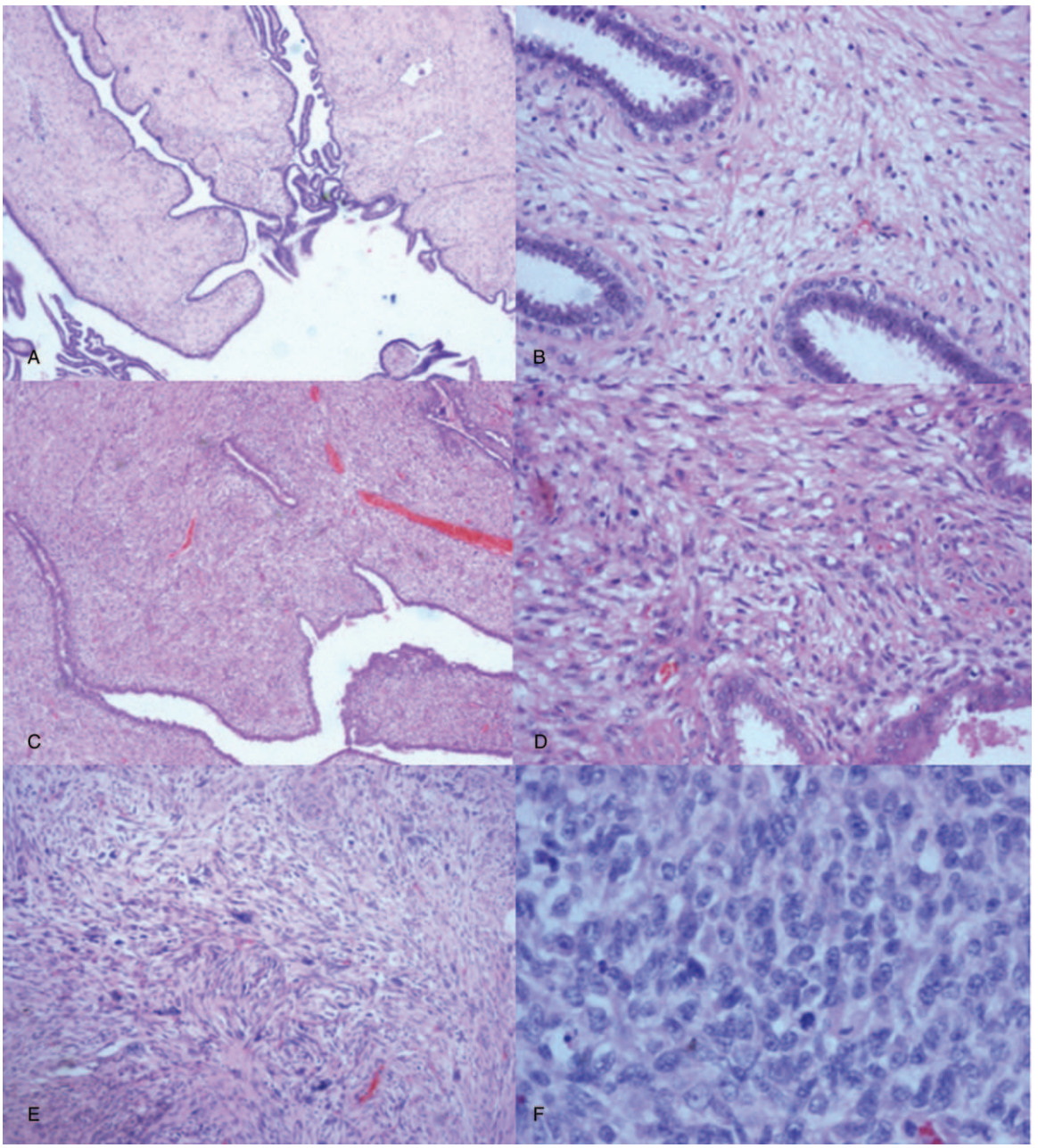

Figure 5. (A) Benign PT with leaf–like fronds and a mild increase in stromal cellularity (40× magnification, H&E). (B) Higher magnification showing the mild increase in stromal cellularity, lack of significant atypia and occasional mitotic figure away from the epithelial component. (100× magnification, H&E). (C and D) Borderline PT with increase in stromal cellularity, mild to moderate atypia and occasional mitoses (40× and 100× magnification, H&E). (E and F) Malignant PT with marked stromal hypercellularity (40× magnification, H&E). Marked nuclear atypia is seen with mitotic figures easily identified (100× magnification, H&E). PT = phyllodes tumor.

Table 4

Surgical management and outcome of patients according to PT subtypes.

	Benign (n = 45)	Borderline (n = 16)	Malignant (n = 15)
Mastectomy	6	12	12
WLE	32	4	2
Excision biopsy	8	0	1
Recurrence	2	1	2

PT = phyllodes tumor, WLE = wide local excision.

components in malignant PTs (80%), albeit a small sample size.[38] In contrast, equal presence of cystic component in all categorization, was seen in another study.[13]

In this study, posterior acoustic enhancement was present in the whole mass or part of it in 85.7% (n = 18) of benign PT, 100% (n = 5) in borderline PT and in 80.0% (n = 8) in malignant PT for patients with available ultrasound images. This was similarly found in a study by Blanco et al[33] where the majority of both benign and malignant PT showed posterior acoustic enhancement in part of the mass or all of it. A total of 5 lesions, 2 of which were malignant, did not demonstrate any posterior

Table 5

ACR BI-RADS lexicon classification 5th Edition 2014.

BIRADS final assessment categories	
Category 0	Mammography: incomplete—need additional imaging evaluation and/or prior mammograms for comparison Ultrasound and MRI: incomplete—need additional imaging evaluation
Category 1	Negative
Category 2	Benign
Category 3	Probably benign
Category 4	Suspicious Mammography and Ultrasound: Category 4a: Low suspicion for malignancy Category 4b: Moderate suspicion for malignancy Category 4c: High suspicion for malignancy
Category 5	Highly suggestive of malignancy
Category 6	Known biopsy-proven malignancy

ACR BIRADS = American College of Radiology Breast Imaging Reporting and Data System, PT = phyllodes tumor.

enhancement, instead posterior shadowing was observed. Hence, the presence of acoustic enhancement or shadowing is not a discerning feature to differentiate the benign, borderline or malignant categorization.

No particular vascularity pattern was observed in any of the PT on ultrasound colour Doppler. This is similar to other studies which showed no significant difference in vascularity between the different PTs.[30,34]

The ACR BI-RADS lexicon classification (Table 5) is a standard reporting guideline that is widely used in the evaluation and categorization of breast lesions (categories: benign, probable benign, suspicious, and highly suspicious of malignancy). Characteristics of lesions in our study were assessed based on the ACR classification, and features that were suspicious or indicated malignancy were looked out for, such as irregular shape, noncircumscribed margins (e.g., spiculated or microlobulated margins), nonparallel orientation, heterogeneous internal echogenicity, and ductal extension on ultrasound, high density, spiculation and amorphous, pleomorphic or linear branching calcifications on mammogram.[6] However, when applied to our study cohort, these findings were not able to conclude a particular distinctive pattern specific to PT as there was an overlap of most of the features in all the tumor subtypes. In view of the close similarity of appearance of PT to fibroadenoma, a more specific characterization would be helpful to differentiate between the 2. Recent studies using shearwave elastography (SWE) where benign and malignant lesions can be quantitatively differentiated by establishing the increased stiffness of nonbenign lesions.[39] Benign lesions are softer than malignant lesions but stiffer or harder than normal breast tissue. It is possible that adding SWE in characterizing the lesions may help to differentiate a fibroadenoma compared to a denser cellular PT.

Three patients had MRI in our study, one of each subtype. In this study, the MRI was indicated for these patients prior to excision for surgical planning and treatment. A study by Tan et al[18] suggested that MRI can be a useful tool for the diagnosis of breast PTs with some of its features such as internal non-enhanced septations, slit-like patterns in enhanced images and signal changes from T2W to enhanced images which correlated significantly with the histologic grade. A high frequency of benign tumors were seen among those with a slit-like pattern in enhanced images.[30] However, this pattern was not observed in our benign PT. All lesions in their study showed hyperintense signal on T2W.[30] On the contrary, only the borderline and malignant PT in our study showed hyperintense signal on T2W sequence, the benign PT showed hypointense signal. 66.7% of the 24 patients in Wurdinger et al's study also showed hypointense signal on T2W sequence,[21] however the subtype was not specified in the study. Lesions that did not show a change in intensity postcontrast on a background of high T2W sequence are likely to be malignant.[44] In view of the small number of patients with MRI in our study, the features for each of the subtype cannot be ascertained. The findings are a mixture of features as noted in different previous MRI studies.[21,30,40–43]

Although the number of patients included in this study was relatively small, detailed information on imaging and pathology features was sufficient considering the follow-up period was between 2 to 7 years.

5. Conclusion

PT is found to be more prevalent among the Malay ethnic group in Malaysia. The ultrasound findings of heterogeneity of lesion, cystic spaces, and posterior acoustic enhancement are common radiological findings. On mammograms, most benign (64.3%) and 33.3% of malignant PT showed high-density lesions. Accurate presurgical core needle biopsy diagnosis can facilitate the type of surgery and treatment management. Surgery, which includes excision biopsy or WLE, is the main treatment option for all subtypes of PT. In the case where the tumor is not feasible for WLE, total mastectomy should be recommended with or without breast reconstruction.

Author contributions

SAH drafted the text of the main manuscript and performed data acquisition and analysis. MTR performed imaging data acquisition and analysis, and prepared Figures 2–5 and Tables 1–4. FF performed the statistical analysis. SJ, SMH and TKH participated in surgical and pathological data acquisition and analysis. KR and NAT jointly supervised the work and revised the manuscript critically. All authors reviewed and approved the final manuscript.

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