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Diagnosis and management of phyllodes tumour of the breast: experience of 33 cases at a specialist centre

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This study reviews the diagnosis and management of a consecutive series of 33 phyllodes tumours of the breast treated at The Royal Marsden Hospital, Sutton, between 1981 and 1992. The mean age of patients at presentation was 41 years (range 15–67 years). Tumours occurred equally in each breast and were significantly more common in the upper outer quadrant ($\chi^2 = 12.7$, df = 3, $P < 0.01$). Clinical features (age, tumour size, palpation) and diagnostic investigations (mammography, ultrasound and fine needle aspiration cytology) were not sufficiently accurate to reliably make a preoperative diagnosis or predict histological type (benign, borderline or malignant). The diagnosis of phyllodes should be considered in patients aged 30–50 years with an apparent fibroadenoma.

Of the patients, 66% underwent wide excision or mastectomy resulting in a favourable local recurrence rate of 14%.

Our experience and review of the literature suggests that adequate local surgery is the treatment of choice and adjuvant treatments have no place in the routine management of phyllodes tumours. Regional lymph nodes were not involved in any of our patients and axillary dissection is not indicated.

Phyllodes tumour is a rare, fibroepithelial tumour of the breast first described as 'cystosarcoma phyllodes' by Müller in 1838 *(1)*. Problems remain in the preoperative diagnosis of phyllodes as lesions are clinically difficult to distinguish from fibroadenomas and investigations such as mammography, ultrasound and fine needle aspiration cytology may not predict histological findings. Local recurrence rates of 40% have been reported after primary surgical treatment *(2)*. The aim of this study was therefore to report experience at a specialist centre and discuss the diagnosis and management of this unusual tumour.

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Patients and methods

A retrospective study was performed of 33 consecutive phyllodes tumours in 32 patients treated at The Royal Marsden Hospital, between 1981 and 1992. Histological confirmation of the disease was obtained in all cases.

Data collected included age, presenting symptom, anatomical site of lesion (side, quadrant), clinical evaluation (palpation, mammography, sonography and fine needle aspiration cytology), surgery performed (local excision, wide excision or mastectomy), tumour size and histological type (benign, borderline or malignant). Follow-up data included survival and incidence of local recurrence or metastatic disease. Mean follow-up was 50 months (range 4–194 months).

Lesions were assessed as benign or suspicious during palpation, mammography and ultrasound examination. Cytological atypia was graded C1–C5 as follows: C1, normal; C2, abnormal, but benign; C3, probably benign; C4, probably malignant; C5, definitely malignant *(3)*. Surgical treatment was determined from the operation notes; wide excision was defined by the recorded intention to obtain 2 cm clearance of the lesion. Tumour size was defined as the maximum transverse diameter measured during macroscopic pathological examination. Histological type was determined from the histopathology records according to the criteria discussed by Azzopardi *(4)* (Table I).

Statistical analysis of observed differences was per-

Table I. Criteria used to assign histological type

	Histological type		
Criteria	*Benign*	*Borderline*	*Malignant*
Tumour margins	Pushing	↔	Infiltrative
Stromal cellularity	Low	Moderate	High
Mitotic rate (per 10 hpf)	<5	5–9	≥10
Nuclear pleomorphism	Mild	Moderate	Severe

hpf, high power field

formed using a one-sample χ^2 test or the Mann–Whitney U test for unpaired scores. A value of $P<0.05$ was considered significant.

Results

The mean age at presentation was 41 years (range 15–67 years). All patients presented with a breast lump and four patients reported associated breast discomfort. Tumours were equally prevalent in each breast and significantly more common in the upper outer quadrant ($\chi^2=12.7$, df=3, $P<0.01$). Mean tumour size was 3.7 cm (range 1.0–18.0 cm). There were no significant associations between histological type, age and tumour size.

Table II describes the clinical findings and results of investigations by histological type. Features recorded as clinically suspicious included lesions with irregular or indistinct margins on palpation ($n=7$) and lesions associated with skin dimpling ($n=1$) and vein reticula ($n=1$). Palpation and radiological investigations were not sufficiently accurate to be reliable in predicting histological type, with only one patient with malignant phyllodes having consistently suspicious results. Fine needle aspiration cytology correctly identified malignancy in two lesions. However, three (12.5%) benign lesions were reported as having grade C3 or C4 atypia. All tumours classified as malignant had at least three relevant diagnostic criteria (Table I).

Table II. Clinical assessment and results of investigations by histological type

	Histological type		
	Benign (n=24)	*Borderline (n=6)*	*Malignant (n=3)*
Palpation			
Benign	20	4	2
Suspicious	4	2	1
Mammography			
Normal	1	0	0
Benign	12	4	2
Suspicious	3	1	1
Not performed	8	1	0
Ultrasound			
Benign	7	2	2
Suspicious	1	1	1
Not performed	16	3	0
Cytology			
C2	18	4	0
C3	2	1	0
C4	1	0	2
Not performed	3	1	1

Table III. Surgical treatment by histological type and tumour size

	Surgical treatment		
	Local excision	*Wide excision*	*Mastectomy*
Histological type			
Benign	10	13	1
Borderline	0	4	2
Malignant	0	0	3
Tumour size (cm)			
<2	6	7	0
2–5	2	8	4
>5	2	2	2

Table III details the surgical treatment by histological type and tumour size. Six patients with an unexpected diagnosis of phyllodes tumour after initial local excision underwent secondary wide excision where margin clearance was suspect. Mastectomy with level 2 axillary dissection was performed in two patients with malignant phyllodes. No nodal involvement was found in either case. Four patients underwent simple mastectomy with simultaneous latissimus dorsi myocutaneous flap reconstruction, one patient with a 4 cm malignant phyllodes and three patients referred for treatment of recurrent phyllodes. The size of lesions treated by mastectomy was significantly larger than those treated by conservative surgery (Mann–Whitney U test, $U=30$, $N_A=6$, $N_B=27$, $P<0.05$). Postoperative radiotherapy was given to the chest wall of one patient with malignant disease.

The characteristics of patients with local recurrence are shown in Table IV. Local recurrence was observed in four patients receiving primary treatment at The Royal Marsden and in four patients referred from other centres. The mean disease-free interval was 22 months (range 4–36 months, $n=8$). No association between local recurrence and histological type or tumour size was observed. All patients with local recurrence had initially undergone conservative surgery (local or wide excision). Three of the patients referred from elsewhere had suspect margins on review of the original histology. Treatment of recurrence was by wide excision in five patients and mastectomy in three patients. No patient has suffered a second local recurrence.

One patient died from metastatic disease arising from an adenocarcinoma of the contralateral breast 46 months after treatment for her phyllodes tumour and one patient required treatment for a synchronous, node positive, contralateral carcinoma.

Table IV. Characteristics of patients with local recurrence

	Royal Marsden (n=4)	*Other centres (n=4)*
Histological type		
Benign	3	2
Borderline	1	2
Malignant	0	0
Primary tumour size (cm)		
<2	2	1
2–5	0	3
>5	2	0
Primary surgery		
Local excision	1	3
Wide excision	3	1
Mastectomy	0	0
Time to recurrence (months)		
<12	1	3
12–24	2	1
24–36	1	0

Discussion

Phyllodes tumour is an unusual fibroepithelial tumour of the breast and represents 0.3–0.9% of all breast tumours *(5)*. The mean age of patients in our series (41 years) is similar to previous reports *(6–9)*. This is some 10–15 years older than the mean age of patients presenting with fibroadenomas *(10)*, but both conditions occur over a wide age range (15–67 years for phyllodes tumours in our series). Tumours show no predilection for side but are more common in the upper half of the breast, particularly the upper outer quadrant (61%). Bilateral tumours are rare (1%) and in our series, one patient had two distinct, synchronous lesions in one breast.

Most patients present with a breast lump, the majority of which are painless and mobile with distinct borders and therefore difficult to distinguish from fibroadenomas. Clinical suspicion of malignancy is greater in older patients, those with a strong family history of breast cancer, those with physical signs such as skin dimpling, vein reticula and those with irregular or indistinct margins on palpation.

The optimal diagnostic and therapeutic procedures are still debated. Mammography typically shows lobulated, benign appearing opacities. Microcalcification is rare *(11,12)*. Mammography reported benign features in six of eight patients with borderline or malignant histology in our series. Ultrasound findings include smooth contours, low level internal echoes, absence of posterior shadowing and intramural cysts *(12,13)*. Ultrasound was performed in only 13 of our patients and, of these, two malignant lesions were reported as benign. Pierart *et al. (14)* report that thermography can distinguish phyllodes from fibroadenomas by demonstrating increased heat generation from the enhanced stromal cell activity seen in phyllodes tumours. Our experience agrees with most reports that palpation, mammography and ultrasound do not allow reliable diagnosis of phyllodes tumours or preoperative prediction of histological type *(11,12,15,16)*.

Fine needle aspiration cytology may be more helpful. In the correct clinical setting, the diagnosis of phyllodes is suggested by the presence of both epithelial and stromal elements, the stroma being present as cellular 'phyllodes fragments' and isolated mesenchymal cells *(17)*. Cytology may be more sensitive in selecting malignant lesions (2/2 ≥ grade C3) and abnormal cytology in lesions thought clinically to be fibroadenomas may encourage appropriate excisional biopsy (3/24 benign lesions ≥ grade C3).

The diagnosis of phyllodes is confirmed by excision and histological examination. Phyllodes tumours have a similar basic structure to intracanalicular fibroadenomas but have a greater degree of stromal cellularity and contain leaf-like or club-like epithelial lined papillary projections pushing into cystic spaces *(3)*. This difference in the connective tissue element is the essential feature distinguishing phyllodes from fibroadenomas, particularly true 'giant fibroadenomas' *(4)* which are often mistaken for phyllodes. Hawkins *et al. (5)* examined the histological features which predict malignant behaviour and found that stromal overgrowth, high stromal cell mitotic activity (≥ 10 mitoses per 10 high power fields), severe nuclear pleomorphism and infiltrating margins were significantly associated with later metastases. The proportion of tumours classified as malignant varies from 1% to 54% in previous reports *(18,19)*, but this proportion depends on the criteria used, interpretation of the connective tissue element and extent of tumour sampling, especially for large tumours which may show variable features. Of the tumours in our series, 9% were classified as malignant. Metastases are haematogenous and usually appear within 5 years of diagnosis, the most common sites being lung, bone and viscera *(19)*. Our series confirms that age and tumour size are not related to histological type *(2,5,16,20)*.

The primary aim of treatment is complete surgical removal of the tumour. Benign phyllodes is often diagnosed unexpectedly after local excision and in these cases, provided that the margins are microscopically clear, a wait-and-see follow-up policy seems justified *(21)*. Routine surgical excision of all lesions thought to be fibroadenomas is unnecessary given the low incidence of phyllodes. Most phyllodes tumours show a relatively fast growth rate *(16)* and it may therefore be sensible to excise breast lumps that have grown significantly at short-term follow-up (3–6 months). Phyllodes tumours do not have a true capsule and should therefore not be enucleated *(22)*, whereas fibroadenoma, including 'giant fibroadenoma', will not recur after complete enucleation. The extent of surgery performed will depend on preoperative suspicion of the diagnosis, tumour size and its relation to breast size, age and patient preferences. Our policy is to perform at least wide excision (2 cm macroscopic clearance) for phyllodes diagnosed preoperatively, for borderline or malignant lesions, and for tumours with involved margins after local excision. Of our patients, 66% underwent wide excision or mastectomy. Six wide excisions were performed as secondary procedures for

suspect margin clearance. Borderline histology may also necessitate further excision. Local recurrence represents failure of primary treatment and reported rates of 0–40% *(2,10,16,21–24)* reflect surgical policy. Local excision runs the risk of unknowingly amputating irregular surface projections, leaving microscopic foci of cells with the potential to form recurrent nodules of tumour. Treatment of recurrent disease may require extensive surgery which may negate any cosmetic benefit derived from minimal primary surgery. Where lesion size is large relative to breast size, wide excision ensuring adequate clearance may mutilate the breast and acceptable cosmesis may be easier to achieve by simultaneous mastectomy and reconstruction. Latissimus dorsi myocutaneous flap with or without nipple preservation is a convenient technique *(25,26)*.

Our policy produced a local recurrence rate of 14% (4 of 29 patients treated for primary lesions) and our data are consistent with reports that local recurrence is more common among patients treated by conservative surgery, but is not associated with histological type, tumour size or age *(2,16,20,26)*. Importantly, local recurrence does not appear to adversely affect survival *(2)*, although recurrences may show less favourable histological characteristics than the primary lesion *(22)*.

In our series, two patients underwent axillary dissection and in neither case was nodal involvement found. The likelihood of nodal metastases is remote and axillary dissection should be reserved for rare cases with clinically evident nodal involvement *(25)*. Adjuvant radiotherapy, chemotherapy and hormone therapy have not proved useful in previous reports, but effective treatment for metastatic disease with combination chemotherapy regimens has been reported in isolated cases *(5,27)*.

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