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Phyllodes tumours of the breast – a retrospective study from 1982–2000 of 50 cases in Portsmouth

W SOTHERAN[1], J DOMJAN[2], M JEFFREY[3], MH WISE[1], PM PERRY[4]

[1]Portsmouth Breast Care Unit, [2]Department of Diagnostic Imaging, and [3]Department of Histopathology, Portsmouth Hospitals NHS Trust, Portsmouth, UK
[4]Academic Department of Surgery, University of Portsmouth, Portsmouth, UK

ABSTRACT

INTRODUCTION This study is a retrospective analysis of 50 phyllodes tumours to determine the optimal surgical procedure for these types of tumours. We have also reviewed rates of recurrence, metastases and mortality based on choice of procedure and histological type.

PATIENTS AND METHODS Cases were ascertained from pathology databases and clinical details extracted from the hospital records. Fifty patients with phyllodes tumours were identified. These comprised 29 benign, 12 borderline and 9 malignant phyllodes tumours.

RESULTS All benign phyllodes tumours were treated with breast-conserving surgery, these included 16 tumours over 40 mm. Borderline and malignant lesions were treated by breast-conserving surgery or mastectomy. The median follow-up period was 35 months (range, 4–96 months). The recurrence rate for all tumours was 14%. Malignant and borderline phyllodes tumours had a recurrence rate of 28%. Tumours excised with a wide margin did not seem to recur. Breast-conserving surgery appeared to be as effective as mastectomy. The choice of procedure was less important than the width of the excision margin. Recurrence occurred in 1/29 benign tumours. Excision margin width did not influence rate of recurrence. One patient died of metastases after mastectomy.

CONCLUSIONS Breast-conserving surgery is the treatment of choice for all benign lesions. For borderline and malignant lesions, excision with a wide margin reduces the rate of recurrence. If a diagnostic local excision biopsy or enucleation is performed, it should be followed by a definitive wider excision.

KEYWORDS
Phyllodes tumours – Breast-conserving surgery – Mastectomy

CORRESPONDENCE TO
WJ Sotheran, Portsmouth Breast Care Unit, Portsmouth Hospitals NHS Trust, Portsmouth, Hampshire PO6 3LY, UK
E: WSotheran@aol.com

Phyllodes tumours are rare, comprising less than 2.5% of all breast cancers[1] and may occur in benign, borderline or malignant forms. The natural history of phyllodes tumours in all forms is unpredictable. Recurrence and metastases have been described in all forms.[2] The authors have reviewed the records of 50 patients treated for phyllodes tumours in Portsmouth hospitals over an 18-year period.

The preferred treatment of phyllodes tumours remains surgical excision. Adjuvant therapy does not appear to be beneficial in the routine treatment of phyllodes tumours.[3] The choice of procedure remains controversial. Many authors advocate mastectomy for large benign and all malignant tumours.[4–7] Other series suggest that breast-conserving surgery may be equally effective in terms of recurrence and metastases.[8,9] Attempts have been made to identify the clinical features which may be associated with a poorer prognosis and, therefore, guide surgical management.[10,11] Histological features which have been correlated with metastatic potential include high tumour grade, stromal overgrowth and tumour necrosis.[12] Other studies have failed to identify characteristics of phyllodes tumours, which may indicate malignant potential.[13]

We sought to determine the incidence of phyllodes tumours in Portsmouth over this period and the rate of pre-operative diagnosis. We have also reviewed, for each tumour type: (i) the surgical management in terms of choice of procedure; (ii) the histological features; (iii) the rate of recurrence; (iv) the incidence of metastases; and (v) mortality from phyllodes tumour. From these indices, we have determined whether breast conserving surgery or

Table 1 Incidence of phyllodes tumour by type and the ages at presentation

Tumour type	Number of cases	Age range (years)
Benign	29	18–65
Borderline	12	20–80
Malignant	9	39–78

mastectomy is the treatment of choice for large or malignant lesions.

Patients and Methods

Cases of phyllodes tumours were ascertained using the pathology data-bases at Portsmouth NHS Hospitals Trust (SNOMED histopathology database); records from 1982 onwards were available. Other cases diagnosed during the course of the study were included. Six cases treated within the private sector were retrieved manually.

The medical records for each patient were reviewed with regard to the pre-operative assessment, surgical management, the histological features of the tumour and recurrence and follow-up.

The surgical management was defined on the basis of the histopathology report:

- **excision** – where tumour was found at or within 1 mm of the excision margin
- **wide local excision** – where the resection margins were greater than 1 mm with breast conservation
- **excision of cavity** – where a wider excision was carried out after excision of tumour
- **mastectomy**.

Histological features of the tumours were reviewed.

Out-patient records were then used to determine the period of follow-up, the rate of recurrence, and metastases and mortality.

Results

Incidence

Fifty cases of phyllodes tumour were identified from 1982–2000 with a median of 2 cases per year (range, 0–11 cases). The incidence for the Portsmouth area was calculated at 0.4 per 100,000 per year. The number of cases diagnosed incidence of each type and ages at presentation are shown in Table 1.

Pre-operative diagnosis

Six of 50 phyllodes tumours were diagnosed pre-operatively. Triple assessment results were available for 22 cases. These lesions were assessed using fine needle aspiration cytology (FNAC), wide bore needle biopsy (WNB), ultrasound scanning assessment (USS) and/or mammography. The diagnostic sensitivity of these investigations, for this series, is shown in Table 2.

Table 2 Use and sensitivity of pre-operative investigation of phyllodes tumours

Investigation	No. of patients	True +ve results	False –ve results	Diagnostic sensitivity
FNAC	37	7	30	0.17
WNB	4	4	0	1
Mammography	40	1	39	0.025
USS	20	3	17	0.17

Surgical management of phyllodes tumours

All 50 lesions were treated by surgical resection. The surgical management of all tumours is summarised in Table 3.

In 37 cases, patients had only one operation. In the remainder, further surgery was carried out after pathological diagnosis.

Histopathology results

In the 41 cases from 1987, the histopathology was reported using criteria as described by Page and Anderson.[14] Cases prior to 1987, 4 benign, 3 borderline and 2 malignant, were reported using contemporary criteria. Size and resection margins were reported consistently. Histological features are shown in Table 4.

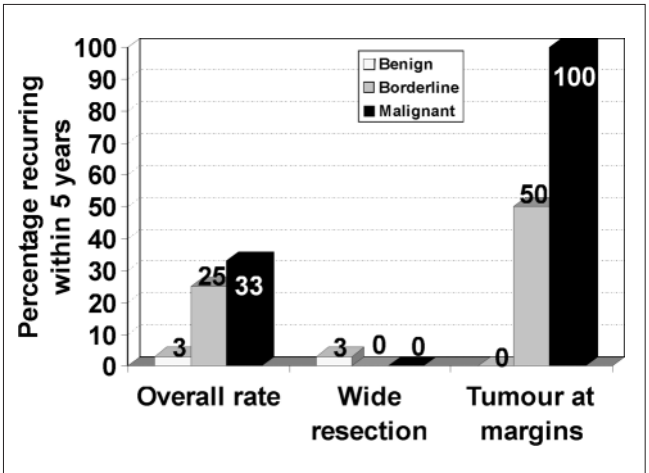

Figure 1 Percentage of patients presenting with recurrence of phyllodes tumour within 5 years.

Table 3 Surgical management of all phyllodes tumours

	Tumour type	First operation	Second operation	Final resection margin	Recurrence interval (months)
1	Benign	WLE		Negative	
2	Benign	WLE		Negative	
3	Benign	WLE		Negative	
4	Benign	WLE		Negative	
5	Benign	WLE		Negative	
6	Benign	WLE		Negative	
7	Benign	WLE		Negative	
8	Benign	WLE		Negative	
9	Benign	WLE		Negative	25
10	Benign	WLE		Negative	
11	Benign	WLE		Negative	
12	Benign	WLE		Negative	
13	Benign	Excision	Excision of cavity	Negative	
14	Benign	Mastectomy		Negative	
15	Benign	Excision		Positive	
16	Benign	Excision		Positive	
17	Benign	Excision		Positive	
18	Benign	Excision		Positive	
19	Benign	Excision		Positive	
20	Benign	Excision		Positive	
21	Benign	Excision		Positive	
22	Benign	Excision		Positive	
23	Benign	Excision		Positive	
24	Benign	Excision		Positive	To Australia at 13[a]
25	Benign	Excision		Positive	
26	Benign	Excision		Unknown	IDC at 48[b]
27	Benign	Excision		Unknown	
28	Benign	Excision		Unknown	
29	Benign	Excision	Excision of cavity	Positive	
30	Borderline	Excision		Positive	
31	Borderline	Excision		Positive	55
32	Borderline	Excision		Positive	3
33	Borderline	Excision		Positive	
34	Borderline	Excision		Positive	
35	Borderline	Excision	Excision of cavity	Negative	
36	Borderline	Excision	Excision of cavity	Negative	
37	Borderline	Excision	Excision of cavity	Negative	
38	Borderline	Excision	Excision of cavity	Positive	25 and 46
39	Borderline	Excision	Mastectomy	Negative	
40	Borderline	Excision	Mastectomy	Negative	
41	Borderline	Mastectomy		Negative	
42	Malignant	Excision		Positive	10
43	Malignant	Excision		Positive	36
44	Malignant	Excision	Excision of cavity	Positive	4
45	Malignant	Excision	Excision of cavity	Positive	
46	Malignant	Excision	Excision of cavity	Negative	
47	Malignant	Excision	Mastectomy	Negative	
48	Malignant	Excision	Mastectomy	Positive	
49	Malignant	Mastectomy		Negative	
50	Malignant	Mastectomy		Negative	

WLE, wide-local excision of tumour; negative, phyllodes tumour at or < 1 mm from resection margin; positive, phyllodes tumour > 1 mm from resection margin. [a]Emigrated 13 months after diagnosis of phyllodes tumour. [b]Presented 48 months later with intraductal carcinoma.

Table 4 Histological characteristics of phyllodes tumours

	Benign	Borderline	Malignant
Number of cases	29	12	9
Positive final resection margins	12	6	3
Range of mitotic indices (mitoses per high power field)	0–4	2–9	5–32
Tumours showing stromal atypia	Not reported	3	5
Median tumour diameter (range) mm	40 (12–100)	45 (17–220)	45 (18–100)

Rates of recurrence

The recurrence rate for all phyllodes tumours was 14%. Recurrence rates by tumour type and by quality of margin are shown in Figure 1.

BENIGN

Twenty-nine benign phyllodes tumour were diagnosed. The median follow-up was 35 months (range, 4–96 months). One patient had recurrence of benign phyllodes tumour (100 x 100 mm), 25 months after wide local excision. This patient had a further wide local excision which has not recurred to date. There were 13 patients known to have tumour at the resection margin following surgery. None of these patients has presented with recurrence in Portsmouth.

BORDERLINE

Twelve borderline phyllodes tumour were diagnosed. The median follow up was 50 months (range, 5–144 months). Three patients developed recurrence. One patient developed recurrence 25 months after local excision, and was treated by subcutaneous mastectomy; a further recurrence 26 months later was treated by mastectomy. Two other patients had recurrence of borderline phyllodes tumour. In both cases, phyllodes tumour was present at the resection margins following initial surgery, and both tumours showed stromal overgrowth. One patient was treated with mastectomy and the other with breast-conserving surgery. Neither has presented with recurrence to date. Three other patients in this group had had positive margins but none has had a recurrence to date.

Two other borderline phyllodes tumours had evidence of stromal atypia or stromal overgrowth on histology. Neither case has presented with recurrence.

MALIGNANT

Nine malignant phyllodes tumour were diagnosed. The median follow-up was 24 months (range, 3–48 months). All three patients with incompletely resected tumour developed recurrence. Stromal atypia was not a consistent feature. Stromal atypia or stromal overgrowth was noted in three other cases of malignant phyllodes tumour. None of these three tumours is known to have recurred.

Metastases

One patient developed metastases. This 78-year-old patient had a mastectomy for a malignant phyllodes tumour, 40 mm in size. The tumour was completely resected with margins > 5 mm. Metastases in the musculoskeletal chest wall developed 18 months after surgery. The patient died shortly after. Stromal overgrowth was not described in the histology.

Mortality

The death of this patient was the only known death from phyllodes tumour in this series.

Discussion

Phyllodes tumours are rare compared with other breast malignancies representing 1–2% of breast tumours seen in Portsmouth hospitals. They have been described in adolescent[15,16] and adult women, with benign tumours tending to affect a younger age group. Their behaviour is poorly understood.

Pre-operative diagnosis of phyllodes tumours remains difficult. Many of the earlier cases in our series pre-date the introduction of routine triple assessment for breast abnormalities. In common with other series, inaccurate pre-operative diagnosis or failure of triple assessment often resulted in local excision of phyllodes tumours, with positive margins, a finding in common with other series.[3]

Since our early cases presented, it is more likely that patients with breast lesions will be assessed in specialist clinic, where triple assessment is standard and core biopsy employed. Further work is needed to determine whether assessment in a dedicated multidisciplinary clinic leads to improved pre-operative diagnosis of phyllodes tumours.

The surgical management of benign phyllodes tumours is local or wide-local excision. Sixteen tumours were > 40 mm in

one or more dimensions. All these lesions were treated with wide-local excision or local excision. Although one case recurred, the recurrence was treated with breast-conserving surgery.

The experience of other centres has led to the proposal that mastectomy is indicated in all patients with large benign lesions.[2,5,6] We would advocate that mastectomy is not mandatory for large benign phyllodes tumours, but may be indicated for cosmetic reasons. The margin of resection of benign phyllodes tumours does not appear to be significant in terms of risk of recurrence. At least 11 of 29 benign lesions were resected with tumour at the resection margin. None of these lesions is known to have recurred.

The treatment of choice for borderline and malignant phyllodes tumours is excision with a wide margin. Where the diagnosis of borderline or malignant phyllodes tumour is made following excision biopsy, this procedure should be followed by a wider excision to reduce the risk of recurrence.

Borderline and malignant tumour type should not be considered an absolute indication for mastectomy rather than wide-local excision. As is evident from Table 3, the choice of procedure for borderline and malignant tumours is less important than the width of the excision margin. Our data suggest that breast-conserving surgery is as successful as mastectomy provided that the tumour is resected with a wide margin. Of patients with borderline lesions, 7/12 were treated with breast-conserving surgery. Malignant tumours were treated in the majority of cases by simple mastectomy but 2/9 were successfully treated by wide-local excision. All patients with recurrence of borderline or malignant phyllodes tumours had margin involvement. The rate of recurrence where the tumour is enucleated or locally excised was 6/9 within 5 years. A recent series of 38 phyllodes tumours showed similar findings.[17] In this series, all patients with recurrence had margin involvement on histological examination, but not all patients with margin involvement developed recurrence.

From our series, recurrence rates were low, after wide-local excision and simple mastectomy.

Two patients had died within 2 years of mastectomy. One patient died from unrelated pathology at 88 years of age and the other patient died of metastases. Fatal metastases following total mastectomy for a phyllodes tumour have been described.[2]

Overall, the recurrence rate in our series was 14%. A comparable series[18] shows an overall rate of recurrence of 14%. Other series show recurrence rates of 7.5%[11] to 14%.[3] Both of these series are smaller with a higher proportion of benign lesions.

Axillary lymph node involvement is exceptional in phyllodes tumours. Our series concurs with the arguments of other authors and suggests that axillary dissection is not indicated routinely in phyllodes tumours.

A follow-up period of 5 years is appropriate for all borderline and malignant lesions as suggested by the recurrence interval in this series, as all the recurrences seen in this series had occurred within 5 years.

Benign tumours were far less likely to recur. However, one patient presented with a malignant phyllodes tumour which was believed to be a malignant recurrence of a benign phyllodes tumour excised previously.

The behaviour of phyllodes tumours is unpredictable. The histological characteristics are not related to their clinical outcome in terms of recurrence, metastases and death. Several studies have attempted to identify predictive parameters.

In the series of Hawkins *et al.*,[12] 72% of cases with stromal overgrowth were observed to metastasise within 5 years. In the Portsmouth series, stromal overgrowth as a predictor of metastatic behaviour is less convincing. Seven phyllodes tumours showed stromal overgrowth but none was observed to have metastasised after a median follow-up period of 36 months (range, 17–96 months). In the patient with metastases, no stromal overgrowth was described.

Mitotic index (MI) did not appear to be significant in predicting the potential for metastatic activity or recurrence. Overall, the average MI was 4.9 (range, 0–32). Six patients had a MI of 8 or greater. One had recurrence after a median follow-up of 35 months (range, 15–108 months). The mean mitotic index of the tumours that recurred was 2.6.

Several studies have examined the relationship between clinical behaviour and the cellular biology of phyllodes tumours.[19,20] High expression of p53 has been associated with other negative prognostic factors,[21] including prominent stromal nuclear pleomorphism, stromal overgrowth and an infiltrative tumour margin.

Conclusions

Local excision or wide-local excision is the treatment of choice for all benign phyllodes tumours. For borderline and malignant lesions, excision with a wide margin reduces the rate of recurrence. If a diagnostic local excision biopsy or enucleation is performed, it should be followed by a definitive wider excision.

High mitotic index and stromal atypia have not been predictive for metastatic behaviour and recurrence, in this series.

Pre-operative diagnosis could be increased with the wider use of wide needle biopsy.

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