The Breast 38 (2018) 52–57

Contents lists available at ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Original article

A retrospective review of phyllodes tumours of the breast: A single institution experience

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ARTICLE INFO

Article history:
Received 15 November 2017
Received in revised form
4 December 2017
Accepted 5 December 2017

Keywords:
Phyllodes tumor
Retrospective
Breast tumor
Prognosis
Treatment

ABSTRACT

Background: Phyllodes tumours are rare and histologically diverse, posing challenges in prognosis and treatment. Due to their rarity, they have seldom been studied.
Purpose: The purpose was to investigate clinical practices in the management of phyllodes tumours, as well as patient outcomes to contribute to the limited body of knowledge surrounding these tumours.
Methods: A retrospective review was conducted on all patients with phyllodes tumours at a single institution. Descriptive analyses were conducted on demographic, disease and treatment (breast-conserving surgery, mastectomy, surgical re-excision, adjuvant/palliative radiation, palliative chemotherapy) information. Overall and disease-free survivals were analyzed, and the cumulative incidence of recurrence and metastases was compared.
Results: 79 patients with phyllodes tumours of the breast were included in the study. Tumours were classified as malignant, borderline, or benign in 67.1%, 21.5%, and 11.4% of patients, respectively. There were no statistically significant differences in overall or disease-free survival between patients with benign, borderline or malignant disease. Only patients with malignant disease developed recurrence or metastases. Those with malignant disease who received mastectomies had a lower 10-year cumulative incidence of recurrence; however this was not statistically significant ($p = 0.69$). All patients had negative surgical margins due to a re-excision or mastectomy following margin-positive breast conserving surgery. Of all risk factors assessed, necrosis was significantly associated with increased incidence of recurrence (local or distant) in patients with malignant disease ($p = 0.03$).
Conclusion: The presence of tumour necrosis is a significant negative prognostic factor. Breast-conserving surgery may be adequate in providing local control, given negative surgical margins.

1. Introduction

Phyllodes tumours (PT) are histologically varied, and can range from resembling benign fibroadenomas to soft-tissue sarcomas [1]. Due to its diverse nature, this rare type of fibroepithelial lesion poses challenges in accurate prognostication and therapeutic management. Several pathological grading systems have been proposed to categorize these tumours. The system adopted by the World Health Organization classifies these tumours as benign, borderline, or malignant with consideration of tumour margins, stromal overgrowth, mitotic rate, cellular atypia, and necrosis [2]. The correlation between histological classification and subsequent biological behaviour of PTs continues to be debated. In their review, Tan et al. noted interpretive subjectivity in grading of these tumours [3].

The National Comprehensive Cancer Network (NCCN) recommends wide excision with margins of at least 1 cm [4]. In the absence of evidence from prospective or randomized studies, routine use of adjuvant radiation is not recommended. The objective of this retrospective review was to investigate clinical practices in the management of PT and patient outcomes at our centre.

2. Methods

A retrospective review was conducted on all patients diagnosed

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https://doi.org/10.1016/j.breast.2017.12.008
0960-9776/

with PT who received treatment at Sunnybrook Odette Cancer Centre. Approval from the institutional research ethics board was obtained prior to initiation of the study. Patients were grouped according to diagnosis (benign, borderline, and malignant). Descriptive analyses were conducted on patient demographics, pathological features, and treatment characteristics. Continuous variables were summarized as mean, standard deviation (SD) and range, and categorical variables were summarized as n and (%).

Overall survival (OS) and disease-free survival (DFS) were calculated and displayed with Kaplan-Meier (KM) curves. The Fine and Gray method was used to calculate and compare cumulative incidence of recurrence and metastases between the subgroups. Using the same method, univariate analyses were also conducted to assess whether pathologic features were related to recurrence metastases. After adjusting for mastectomy or lumpectomy treatment, multivariable analysis was performed with significant factors which were found in the univariate analysis. $P < 0.05$ was considered statistically significant.

3. Results

A total of 79 patients diagnosed with PTs of the breast were treated at the Sunnybrook Odette Cancer Centre from 1999 to 2017. Tumors were classified as malignant in 53 patients (67.1%), borderline in 17 patients (21.5%) and benign in 9 patients (11.4%) (Table 1). The average age of patients was 48.9 years. Ten patients (12.7%) reported a prior diagnosis of PT, and 12 (15.2%) indicated previous benign breast tumours (e.g. fibroadenoma). Patients with benign tumours were followed for a median of 3.04 years (range 0.91–8.52 years). Patients with borderline tumours were followed for a median of 5.53 years (range 0.12–10.83 years). Patients with malignant tumours were followed for a median of 4.15 years (range 0.20–10.91 years).

A minority of patients ($n = 26$) were treated before 2008. There were no significant temporal differences in patterns of practice. A total of 61 patients underwent lumpectomies, of which 18 received a re-excision and 18 received subsequent mastectomies due to unclear margins. Thirty-four patients underwent mastectomies initially due to tumor size. Adjuvant radiation was given to 34 patients (43.0%), of which 8 received an additional boost. Adjuvant radiation (50 Gray [Gy] in 25 fractions) was given to patients with benign ($n = 2$) and borderline ($n = 3$) disease in cases of presumed recurrent PT.

Most patients with malignant PT (58.5%) underwent a mastectomy, and all other patients received breast conserving surgery (41.5%). Of the 29 patients with malignant disease who received adjuvant radiation, most received 50Gy/25 ($n = 27$, 93.1%).

One patient received 4 cycles of adjuvant Adriamycin DTIC due to a history of multiple benign PTs. Another patient received hypofractionated radiation with Cisplatin due to poor prognostic factors and rapid recurrence post-mastectomy (<2 months). All other chemotherapies were given with palliative intent following metastases. First line treatments consisted of doxorubicin, ifosfamide (with doxorubicin or etopiside), and triple-combination chemotherapy consisting of cyclophosphamide, methotrexate, fluorouracil (CMF). Three patients received second line palliative treatments, consisting of docetaxel or gemcitabine monotherapies, or combination treatments with cisplatin, etopiside and ifosfamide.

There were no statistically significant differences in OS ($p = 0.10$, Fig. 1) and DFS ($p = 0.11$, Fig. 2) between patients with benign, borderline or malignant disease. In patients with malignant disease, 1- and 5-year OS were 93.9% and 78.9% respectively; and 1- and 5-year DFS were 87.9% and 80.6% respectively.

Only patients with malignant disease developed recurrence

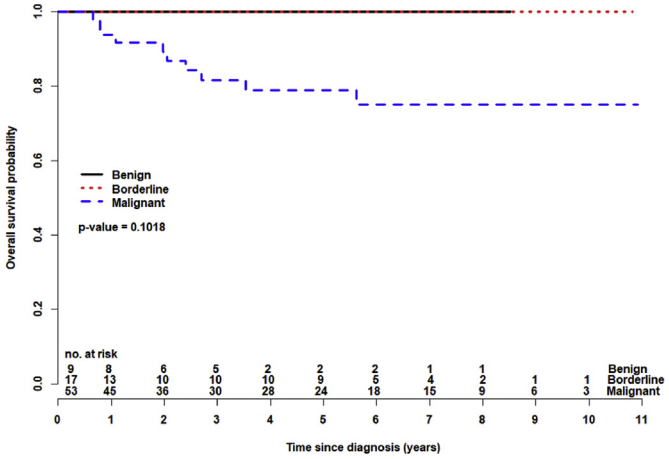

Fig. 1. Kaplan-Meier overall survival curve for benign, borderline and malignant phyllodes tumours.

Table 1
Patient and disease characteristics.

	Types of Phyllodes Tumors		
	Benign ($n = 9$)	Borderline ($n = 17$)	Malignant ($n = 53$)
Patient characteristics			
Age at diagnosis (years)			
Mean ± SD	45.11 ± 16.04	49.00 ± 11.26	49.53 ± 11.48
Min, Max	23.00, 77.00	31.00, 70.00	24.00, 88.00
Duration of follow-up since diagnosis (years)			
Median (range)	3.04 (0.91–8.52)	5.53 (0.12–10.83)	4.15 (0.20–10.91)
Previous diagnosis of PT	0 (0.00%)	4 (23.53%)	6 (11.32%)
Previous benign breast tumor	4 (44.44%)	1 (5.88%)	7 (13.21%)
Treatment			
Surgery			
Breast conserving surgery	7 (77.78%)	16 (94.12%)	22 (41.51%)
Mastectomy	2 (22.22%)	1 (5.88%)	31 (58.49%)
Adjuvant radiation	2 (22.22%)	3 (17.65%)	29 (54.72%)
Boost	0 (0.00%)	0 (0.00%)	10 (18.87%)
Chemotherapy	0 (0.00%)	0 (0.00%)	8 (15.09%)
Adjuvant	N/A	N/A	2 (25.00%)
Palliative	N/A	N/A	6 (75.00%)

Abbreviation: phyllodes tumours, PT; standard deviation, SD.