

Radiotherapy in Phyllodes Tumour

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ABSTRACT

Introduction: Phyllodes Tumour (PT) of the breast is a relatively rare breast neoplasm (<1%) with diverse range of pathology and biological behaviour.

Aim: To describe the clinical course of PT and to define the role of Radiotherapy (RT) in PT of the breast.

Materials and Methods: Retrospective analysis of hospital data of patients with PT presented from 2005 to 2014 was done. Descriptive statistics was used to analyze the results. Simple description of data was done in this study. Age and duration of symptoms were expressed in median and range. Percentages, tables and general discussions were used to understand the meaning of the data analyzed.

Results: Out of the 98 patients, 92 were eligible for analysis. The median age of presentation was 43 years. A total of 64/92 patients were premenopausal. There was no side predilection for this tumour but 57/92 patients presented as an upper outer quadrant lump. Fifty percent of the patients presented as giant

(10 cm) PT. The median duration of symptoms was 12 months (range: 1-168 months). A 60% of patients had Benign (B), 23% had Borderline (BL) and 17% had malignant (M) tumours. The surgical treatment for benign histology included Lumpectomy (L) for 15%, Wide Local Excision (WLE) for 48%, and Simple Mastectomy (SM) for 37%. All BL and M tumours were treated with WLE or SM. There was no recurrence in B and BL group when the margin was ≥ 1 cm. All non-metastatic M tumours received adjuvant RT irrespective of their margin status. Total 3/16 patients with M developed local recurrence. Total 6/16 M patients had distant metastases (lung or bone). Our median duration of follow up was 20 months (range: 1-120 months).

Conclusion: Surgical resection with adequate margins (>1 cm) gave excellent local control in B and BL tumours. For patients with BL PT, local radiotherapy is useful, if margins are close or positive even after the best surgical resection. There is a trend towards improved local control with adjuvant radiotherapy for malignant PT. Metastatic malignant PT has a poor outcome.

Keywords: Borderline phyllodes tumour, Malignant phyllodes tumour, Postoperative radiotherapy, Simple mastectomy, Wide local excision

INTRODUCTION

Phyllodes tumours are rare fibro-epithelial neoplasms of breast which accounts for less than 1% of all breast neoplasms [1]. This tumour was first described by Johannes Muller who coined the term cystosarcoma phyllodes [1]. The World Health Organization (WHO) has classified these tumours into benign, borderline and malignant subtypes based on the frequency of mitosis, infiltrative margins, degree of stromal cellular atypia, cellularity, degree of stromal overgrowth and margin appearance [2,3]. PT has a diverse clinical and pathological behaviour. The clinical course of PT may not correlate exactly with its histological parameters. Surgery is the treatment of choice for PT [4]. Benign and borderline PT can be cured with adequate surgical resection. The risk of local recurrence was low in benign tumours and appreciably high in BL tumour [4]. In view of the rarity of this tumour, there are no randomized controlled trials to establish a standard management protocol for these types of tumours and these remains as a poorly understood tumour of the breast. We conducted a retrospective review of hospital records of patients with PT who were treated in our center in the last 10 years. The aim of this retrospective review was to define the role of radiotherapy in PT of breast.

MATERIALS AND METHODS

This is a retrospective analysis of hospital data of patients with PT presented from January 2005 to December 2014. This study was started after approval from the institutional review board of Christian Medical College and Hospital (CMC), Vellore, Tamil Nadu, India. Records of the all patients with a histological diagnosis of PT, who underwent treatment at CMC, Vellore, during this time

duration, were included in the trial. We collected data on patient related factors like age at presentation, menopausal status, site of the lesion, presence of any comorbid conditions, tumour related factors like size at presentation, resection margin status, treatment factors like type of surgery, adjuvant radiotherapy and histological factors like benign, borderline or malignant tumour. The disease status at the last follow up visit was noted. Descriptive statistics was used to analyze the results.

RESULTS

Patient Characteristics: Ninety eight patients with FNAC/trucut biopsy report of PT were seen in our outpatient clinic from January 2005 to December 2014. Five patients were excluded because the final histopathology report came as fibro adenoma. One patient was excluded as she refused any treatment for PT. Thus, 92 patients were eligible for the final analysis. Age of our patient population ranged from 22 to 77 years (median age was 43 years). Almost, 58% of our patients were in the fourth and fifth decades of life. A 69% were premenopausal, 26% were post-menopausal and menopausal status was not known for 5% patients. A 53% presented with right breast lump and 47% with left breast lump. The most common presentation was that of a painless slow progressive lump. A total of 45% patients presented as giant PT (>10 cm). The largest tumour size in this group was 25 cm. Nearly, 20% (19/92) patients presented to us as recurrent breast lump. The duration of symptoms ranged from 1-168 months with a median of 12 months. A 12% of these patients underwent lumpectomy, 41% WLE and 47% underwent SM. A 60% of our tumours were Benign (B), 23% were Borderline (BL) and 17% were Malignant

(M). Patient characteristics are listed in [Table/Fig-1].

Benign Phyllodes Tumour (B): Fifty five patients (60%) had benign PT. Nine patients underwent lumpectomy (L), 26 patients underwent WLE and 20 patients underwent SM. The median follow up for this patient group was 24 months. Adjuvant radiation therapy was not offered for benign PT. Five out of 55 patients developed local recurrence. The time for local recurrence ranged from 10 to 69 months in our patient cohort. The patients who had local recurrence had surgical resection margin <1 cm. They underwent surgery with adequate margins at the time of recurrence. All patients with benign PT were alive and disease free at their last follow up visit.

Borderline Phyllodes Tumour (BL): Twenty one patients in our cohort were having borderline PT. A total of 9/21 underwent WLE and 12/21 had SM. A total of 9/21 patients had less than adequate margin. Seven out of nine patients received adjuvant radiation therapy. One patient with inadequate margin underwent re-surgery (simple mastectomy). Local recurrence occurred in one patient eight months after a WLE where the deep resection margin was 0.1 cm. This patient underwent a re-excision with a margin of 1.5 cm. All patients with borderline PT were alive and disease free at the time of their last follow up.

Malignant Phyllodes Tumour (M): Sixteen patients presented with malignant PT. A total of 15/16 patients presented as giant PT. A total of 13 patients underwent SM, two had WLE and one had lumpectomy. The patient who underwent lumpectomy alone had a tumour size of 4 cm at presentation and was alive and disease free with a follow up of 64 months. Nine patients received post operative radiation therapy. The RT dose was 50 Gy in 25 fractions to the chest wall or whole breast. Six patients had metastases and they received chemotherapy. Lung was the most common site of metastasis followed by bone. The chemotherapy regimen used was either a combination of cisplatin/doxorubicin or single agent doxorubicin.

Our median duration of follow up for malignant PT cohort was 19 months (range: 2-186 months). Median overall survival of patients who developed metastases was seven months. Three patients had local recurrence. Two patients presented to us as local recurrence after WLE alone. They underwent SM at recurrence followed by radiotherapy to chest wall. One patient developed local recurrence after radiotherapy. She underwent excision of the local recurrence. The median time to develop local recurrence was 14 months (range: 10-36 months). The treatment outcome of benign, borderline and malignant PT is listed in [Table/Fig-2].

DISCUSSION

Majority of the PT occurred in women between the ages of 35-55 years [4]. PT is reported rarely in men. Our patient population was

Patient Characteristics	
N	92
Age	Median: 43 years, Range: 22-77 years
Menopausal status	Premenopausal: 64 (69%) Postmenopausal: 24 (26%) Unknown: 4 (5%)
Side	Right: 49 (53%) Left: 43 (47%)
Size	>10 cm (Giant PT) – 41(44.5%) ≤ 10 cm – 46 (50%) Size not documented: 5(5.5%)
Duration of symptoms	Range: 1 – 168 months, Median: 12 months
Histology	Benign: 55 (60%) Borderline: 21 (23%) Malignant: 16 (17%)

[Table/Fig-1]: Patient characteristics.
PT: Phyllodes tumour

only women and the age ranged from 22-77 years. PT usually presents as a lump in the breast for several years with sudden increase in size. Reinfuss M et al., proposed that benign PT can be treated with wide local excision with a margin of 1 to 2 cm all around [4]. Our results also concur with this finding. We noted that if the surgical margins are ≥1 cm, there was no local recurrence. All local recurrences we had in B and BL groups had a surgical margin <1 cm. Breast conservation is preferred whenever possible. Abdalla HM et al., stated that the histotypes of tumour and resection margins were the principal determinants of local recurrence and distant metastases in PT [5]. The surgical resection with adequate

Variables	Benign (B)	Borderline (BL)	Malignant (M)
No. of patients	55	21	16
Type of surgery			
L	9	0	1
WLE	26	9	2
SM	20	12	13
Adjuvant RT	No	7 patients	9 patients
Median follow up	24 months	18 months	19 months
Local recurrence	5	1	3
Treatment at recurrence	Re-surgery with adequate margin	Re-surgery with adequate margin	Re-surgery and radiotherapy
Distant metastases	nil	nil	Yes

[Table/Fig-2]: Treatment outcome of the benign, borderline and malignant phyllodes tumour with surgery and radiotherapy.

margin is the primary treatment of PT. Axillary Lymph Node (LN) dissection is not routinely indicated as the incidence of axillary LN metastases is very rare (<1%) [2]. Cohn-Cedermark G et al., in his clinicopathologic review of 77 patients with PT has stated that optimal treatment of PT is resection with at least 1 cm margin all around, particularly in BL and M type [6]. The choice of surgery (L vs. WLE vs. SM) depends on the size of the tumour [6]. Chen W-H et al., in his surgical series recommended that routine axillary LN dissection is not recommended for PT [7]. Axillary dissection was not done for any of the patients in this retrospective cohort.

Surgery is the primary modality of treatment in patients with malignant PT of the breast. The extent of surgery and the role of adjuvant radiotherapy remain controversial. We had sixteen patients with malignant PT. Simple mastectomy was the preferred surgical option for this group, mainly because 94% of our patients presented as giant PT. All patients with non-metastatic malignant PT received adjuvant RT irrespective of the margin status. The dose delivered was 50 Gy in 25 fractions to the chest wall or whole breast. There were three local recurrences in this group. Two patients presented to us with local recurrence after a WLE done at their hometown for M PT. One patient had local recurrence after SM and chest wall radiotherapy. This patient had a tumour size of 25 cm at presentation and had a close surgical resection margin. Mitus J et al., in his series on malignant PT mentioned that mastectomy is indicated only if tumour-free margins cannot be obtained by breast conservation surgery and adjuvant radiotherapy may be considered if tumour free margins are <1 cm [8]. We feel that a dose more than 50 Gy is required for adequate local control, if margins are close. Belkacemi Y et al., mentioned that tumour size has prognostic significance in M PT [9]. In his series, a tumour size <3 cm was associated with a better outcome. We noticed that 94% of our patients with M PT had a tumour size more than 10 cm. A large tumour demands simple mastectomy for adequate margins. Guillot E et al., noticed that the risk of local recurrence increases with increase in tumour size [10]. Barth RJ et al., in their prospective study of adjuvant radiotherapy for malignant PT mentioned that adjuvant radiotherapy is very effective for local control of BL and M PT [11]. Re-excision was done for positive margins after initial excision. Margin negative patients received

adjuvant radiotherapy irrespective of their margin size. There was no local recurrence with adjuvant radiotherapy in this group of patients [11].

A total of 6/16 patients with M PT had metastases. One reason for high incidence of metastases is that our patient group had more poor prognostic tumours in view of large tumour size. The patients who had metastases were treated with chemotherapy. Two patients with lung metastases died during treatment. The other four patients who completed their chemotherapy were lost to follow up.

The role of hormonal therapy in the treatment of PT is unknown. Chemotherapy is tried for metastatic malignant PT, but the response documented is of short duration [12]. Hawkins RE et al., stated that the most reliable predictor for metastases was stromal overgrowth [12]. He stated that the risk of metastases in patients with a high degree of stromal overgrowth was 75%. Cisplatin and doxorubicin based chemotherapy was given for patients with metastatic malignant PT. But the chemotherapy was not well tolerated.

LIMITATION

This is a retrospective study to assess the tumour control in patients with PT who were treated with or without post operative radiotherapy in our center. There is no control arm in this study. Hence, we cannot make definite comparison of outcome between radiated and non-radiated patients. We can only suggest that there is a trend towards improved outcome with radiotherapy in patients with risk factors.

CONCLUSION

Surgical resection with adequate margins (>1 cm) gave excellent local control in B and BL tumours. For patients with BL PT, local

radiotherapy is useful, if margins are close or positive even after the best surgical resection. There is a trend towards improved local control with adjuvant radiotherapy for malignant PT. Metastatic malignant PT has a poor outcome.

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