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Original Article

A Retrospective Review of Phyllodes Tumor of Breast Treated with Multimodality Approach: Experience of a Tertiary Care Institution in Eastern India

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Abstract

Background: The cornerstone of management of phyllodes tumor is surgery. No standard of care exists regarding adjuvant therapy; however, local recurrence is a predominant pattern of failure. The aims of this study were to evaluate the clinical characteristics and treatment patterns of phyllodes tumor and to compare local recurrence and disease-free survival rates of patients with borderline and malignant phyllodes tumor treated with or without adjuvant radiotherapy. **Materials and Methods:** We analyzed the demographic data, treatment details, and recurrence patterns of all patients with nonmetastatic phyllodes tumors of the breast (n = 34) treated with a multimodality approach who presented to our institute from January 2015 to December 2020. **Results:** The median age at presentation was 41.2 years, and the median tumor size was 12.5 cm. All patients underwent definitive surgical procedures in the form of wide local excision or mastectomy. No recurrence was noted in the patients with a benign histology. After a median follow-up period of 38 months, the local recurrence rate was 27% for the patients with borderline and malignant histology treated with adjuvant radiotherapy (n = 11) versus 47% for those (n = 17) who did not receive adjuvant radiotherapy. The 3-year local recurrence-free survival rate was 72% in the adjuvant radiotherapy group, versus 51% in the surgery only group. **Conclusion:** The results of the current study confirm the excellent prognosis of patients with benign phyllodes tumor undergoing surgery alone. Local recurrence was the predominant mode of failure in the patients with borderline and malignant histology. Locoregional control was improved with the addition of postoperative radiotherapy in the patients with borderline and malignant histology irrespective of margin status.

Keywords: Adjuvant radiotherapy, borderline phyllodes, breast tumor, malignant phyllodes, phyllodes tumor

Introduction

Phyllodes tumor of the breast is a rare fibroepithelial lesion comprising 0.3%–0.5% of female breast tumors.[1] The incidence of the tumor is 2.1 per million, and it usually occurs

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in females aged 42–45 years,[2,3] which is about 15–20 years later than the usual presentation with fibroadenoma of the breast.[4] Phyllodes tumor of the breast is comparatively rare among adolescents and the elderly. The term cystosarcoma phyllodes, which is the benign variant of phyllodes tumor, was coined by Johannes Muller[5] in 1838, due to the cystic, fleshy, and leafy gross appearance of the tumor. The metastatic, or rather malignant counterpart, was reported by Lee and Pack in 1931.[6] In 1981, the WHO adopted the term phyllodes tumor.

Phyllodes tumors are classified into benign, borderline, and malignant grade categories depending on the degree of stromal cellularity and atypia, mitotic count, stromal overgrowth, and nature of the tumor margins.[7] The overlap between fibroadenoma and phyllodes raises the question of pathological kinship. The stromal elements play a key role in distinguishing phyllodes tumors from fibroadenomas and benign tumors from malignant phyllodes tumors.[8]

Clinically phyllodes tumor often presents as a rapidly growing breast lump. Nipple retraction and ulceration are uncommon, and it is rarely bilateral. The median size of a phyllodes tumor is around 4 cm, and 20% of tumors grow larger than 10 cm (arbitrary cutoff size for the designation of a giant phyllodes tumor). They have been reported to reach a maximum size of 40 cm.[9]

Phyllodes tumors are usually treated with local surgical excision with tumor-free margins of 1 cm or greater.[10] Lumpectomy or partial mastectomy is the preferred surgical therapy. Total mastectomy is necessary only if negative margins cannot be obtained by lumpectomy or partial mastectomy.[11] Since phyllodes tumors rarely metastasize to the axillary lymph nodes, surgical axillary staging or axillary lymph node dissection is not usually performed unless clinically indicated.[12]

The role of adjuvant radiotherapy in the management of phyllodes tumor is controversial, and no further adjuvant treatment is warranted after margin-negative surgical resection of benign phyllodes tumors.[13] However, in borderline and malignant tumors, a few retrospective studies have reported favorable outcomes with adjuvant radiotherapy, particularly when a wide resection margin was not achieved during surgery.[14,15]

The present analysis was undertaken to review our institutional experience with phyllodes tumors and to investigate clinical practice in the management of these uncommon and unpredictable breast tumors. This retrospective analysis includes long-term outcomes in terms of local recurrence and disease-free survival (DFS) rates.

Materials and Methods

A retrospective audit of all patients with phyllodes tumor who presented from January 2015 to December 2020 to the radiotherapy department of a tertiary care hospital in Kolkata was undertaken. The study received ethical clearance from the IPGME and R Research Oversight Committee (Institutional Ethics Committee for research involving human participants), with IRB Number: IPGMER/IEC/2022/081. Histopathologically proven cases of phyllodes tumor who underwent curative treatment in the form of surgery alone or followed by adjuvant radiation were considered. Data were collected with regard to age, presentation, histological diagnosis, treatment, recurrence, and follow-up details. Thirty-six patients presented with phyllodes tumors during the study period, of whom 2 were lost to follow-up. The remaining 34 patients were analyzed. Adjuvant radiotherapy was defined as any radiation received after the first or subsequent radical surgery. Disease-free interval was calculated from date of definitive surgery.

Descriptive analyses were conducted on patient demographics, pathological features, and treatment characteristics. Continuous variables were summarized as mean and range; categorical variables were summarized as *n* and percentage (%). Local recurrence-free survival and DFS rates were calculated and displayed with Kaplan–Meier curves.

Results

All of the 34 patients were treated with definitive surgical procedures. The tumors were classified as being malignant in 19 (56%) patients, borderline in nine (26%) patients, and benign in six (18%) patients. The average age of the patients was 41.2 years. Seven (21%) patients presented with recurrent phyllodes tumors, of whom 6 had malignant phyllodes tumors [Table 1].

Five (15%) of the 34 patients underwent breast conservation surgery, and 29 (85%) patients underwent mastectomy at

Table 1: Patient, tumor and treatment characteristics stratified according to the pathologic subtype.

	Subtypes of phyllodes tumors		
	Benign (*n*=6)	Borderline (*n*=9)	Malignant (*n*=19)
Age at diagnosis (years)			
Median	42.5	36	46
Min, max	22, 50	18, 46	24, 68
Disease status at presentation			
1st Presentation	5 (83%)	9	13 (68%)
Recurrent	1 (17%)	0	6 (32%)
Surgery			
BCS	1 (16%)	1 (11%)	3 (16%)
Simple mastectomy	4 (67%)	4 (44%)	6 (32%)
MRM	1 (16%)	4 (44%)	10 (52%)
Tumor size (cm)			
Median (range)	13 (6-17)	11 (6-15)	12.8 (7-24)
Adjuvant radiotherapy	1 (positive margin and no scope of resurgery)	2	9
Chemotherapy adjuvant	Nil	Nil	5

initial presentation due to the large size of the tumor. The average maximum dimensions of the malignant, borderline, and benign phyllodes tumors were 13 cm, 11 cm, and 12.8 cm, respectively [Table 1]. Of these 29 patients, 15 underwent additional axillary dissection. Margins were positive in eight (24%) patients, close in four (12%) patients, and free in 20 (59%) patients. Margin status was unknown in two patients. Of the 15 patients who underwent axillary dissection, none had positive axillary lymph nodes.

Adjuvant radiotherapy was given to 12 (35%) of the 34 patients, of whom 9 had malignant tumors and 2 had borderline tumors. Only one patient with benign histology was treated with adjuvant radiotherapy in view of positive margins for which revision surgery was not possible. Four (36%) of 11 patients with malignant and borderline histology who received adjuvant radiotherapy had either close or positive margins. Six (35%) of 17 patients with malignant and borderline histology who did not receive adjuvant radiotherapy had close or positive margins [Table 2]. All patients received at least 50 Gy in conventional fractionation except for 1 who was treated with a hypofractionated regimen. One patient received an additional 10 Gy boost to the tumor bed.

Five of the 34 patients received adjuvant chemotherapy, all of whom had malignant histology [Table 1]. The patients usually received 6 cycles of chemotherapy and a combination chemotherapy based on alkylating agents and anthracyclines was preferred.

After a median follow-up of 38 months, nine (47%) patients with malignant histology and 2 (22%) with borderline histology developed local recurrence [Table 3]. No local recurrence was noted in the patients with benign phyllodes. Two patients with malignant phyllodes developed lung metastasis in the absence of local recurrence [Table 3]. Further staging workup in 8 patients who developed local recurrence revealed the presence of distant metastasis, and they were mostly treated with palliative chemotherapy. The response to palliative chemotherapy was dismal, and the patients died 3–9 months after the detection of distant metastasis.

Three (27%) of 11 patients with a high-risk variety (malignant or borderline histology) who were treated with adjuvant radiotherapy developed local recurrence. Eight (47%) of 17 patients with a similar histology who did not receive adjuvant radiotherapy developed local recurrence [Table 4]. The patients who received adjuvant radiotherapy had better 3-year local recurrence-free survival [Figure 1] compared to the patients who did not (72% vs. 51%, P = not significant). The 3-year DFS rate in the adjuvant radiotherapy group was 64% versus 47% in the surgery only group, although the difference was not statistically significant [Figure 2].

Table 2: Patient, treatment and tumor characteristics stratified according to radiotherapy administration in borderline/malignant phyllodes tumors.

	Adjuvant radiotherapy (n=11)	No adjuvant radiotherapy (n=17)
Age (years)		
Median (range)	46 (28-55)	40 (18-68)
Type of surgery		
BCS	1 (09%)	3 (18%)
Mastectomy	5 (45%)	5 (29%)
MRM	5 (45%)	9 (53%)
Tumor size (cm)		
Median (range)	10 (19-6)	13 (24-7)
Margin		
Free	6 (54%)	10 (59%)
Close	2 (18%)	2 (12%)
Positive	2 (18%)	4 (24%)
Unknown	1 (09%)	1 (06%)

BCS- Breast conserving surgery, MRM- Modified radical mastectomy

Table 3: Results according to pathological subtypes

	Benign (n=6)	Borderline (n=9)	Malignant (n=19)
Median follow-up duration (month)	30	37.5	38
Local recurrence (percentage)	nil	2 (22%)	9 (47%)
Distant metastasis	nil	nil	2
Salvage surgery	-	1	1
Salvage chemotherapy	-	1	5

Table 4: Treatment outcome stratified according to radiotherapy administration in borderline/malignant phyllodes tumors.

	Adjuvant radiotherapy (n=11)	No adjuvant radiotherapy (n=17)
Median follow-up duration (month)	38	31
Local recurrence	3 (27%)	8 (47%)
Distant metastasis	1	1
Salvage surgery	nil	2
Salvage chemotherapy	3	3

Discussion

Phyllodes tumors are rare fibroepithelial breast tumors with diverse biological behavior occurring in relatively young women compared with adenocarcinoma of the breast. In our study, the median age at presentation was 41.2 years, which is comparable with worldwide statistics.[3,16,17] The median tumor size was 12.5 cm, which is consistent with the findings of Mallick *et al*.[18] The largest tumor size in our series was 24 cm [Figure 3], representing a giant phyllodes tumor. However, in developed countries, the median size is 4–7 cm.[9,16] This reflects delayed presentation in the Indian population.

Only 18% of our patients presented with benign phyllodes, while in many series, benign phyllodes has accounted for 50% of phyllodes tumors. This may be explained by the reluctance

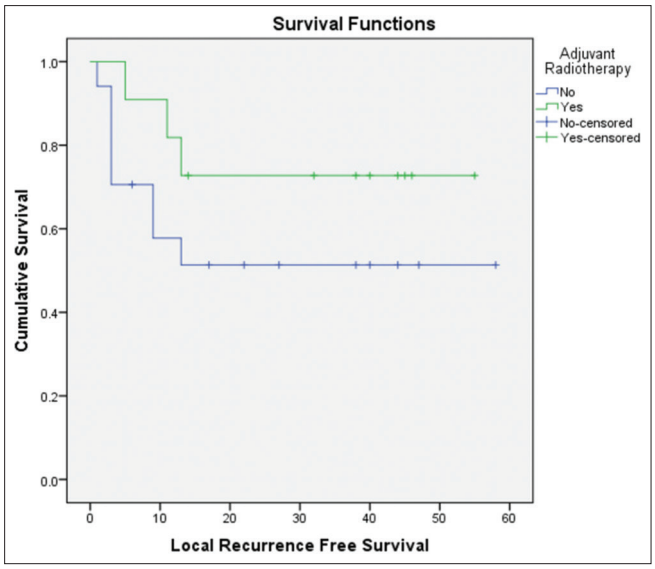

Figure 1: LRFS in relation to adjuvant radiotherapy administration in the borderline/malignant group. LRFS: Local recurrence free survival

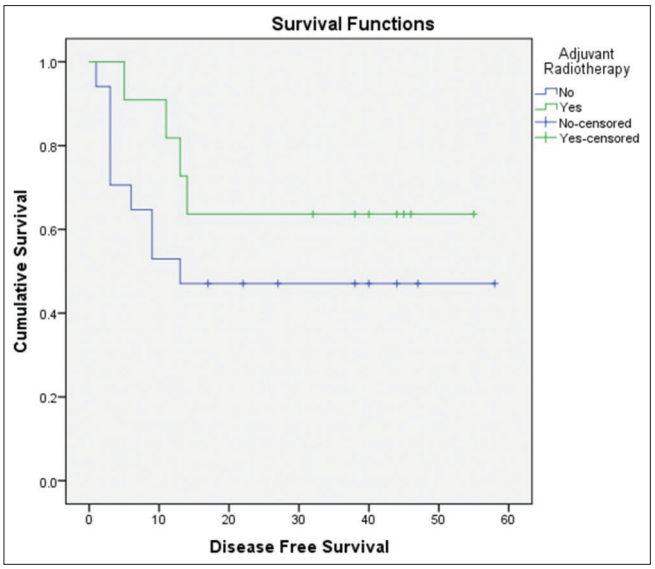

Figure 2: DFS in relation to adjuvant radiotherapy administration in the borderline/malignant group. DFS: Disease free survival

of general surgeons operating on benign phyllodes to refer patients to radiation oncology departments for follow-up, since the perceived risk of recurrence is low among this group.

In our cohort, 5 (15%) patients underwent breast conserving surgery. The median tumor size in these cases was 14 cm. Barth *et al*. reported that breast conserving surgery was a successful modality for surgical management in tumors with a mean size of 3.7 cm.[14] In our series, margins were close/positive in three patients, and none were re-excised. All three patients developed recurrence, which suggests a more judicious selection of breast conserving surgery over mastectomy. Of the 29 patients who underwent mastectomy, 15 were treated additionally with axillary dissection, and none showed any lymph node involvement. Phyllodes tumor is not known to metastasize to the regional lymph nodes,[8,19,20] and hence multiple reaction monitoring should only be reserved for clinically detected positive axillary node cases.

Adjuvant radiotherapy decreased the likelihood of local recurrence in our patients with borderline/malignant histology. In these patients, the rate of local recurrence in those treated with adjuvant radiotherapy was 27% (3 of 11 patients) compared to 47% (8 of 17 patients) for those who did not receive radiotherapy. Several studies have described the successful use of adjuvant radiotherapy in small numbers of patients after margin-positive mastectomies.[11,21,22] In these studies, adjuvant radiotherapy was used only for close margin or positive cases. However, in our study, the benefit of adjuvant radiotherapy was seen irrespective of the margin status, as both patients with close and positive margins were equally distributed in surgery only and surgery plus adjuvant radiotherapy groups (35% vs. 36%). The only prospective study available to date by Barth *et al*.[14] demonstrated that margin-negative wide local excision combined with adjuvant radiotherapy was an effective therapy for the local control of borderline and malignant phyllodes tumors.

After a median follow-up of 38 months, the local recurrence rate was 32%, which is higher than the recurrence rate reported in previous studies (8%–19%).[23-25] Our findings can be explained by the fact that the proportion of patients with benign histology was much lower compared to the other histologic subtypes. Two patient developed distant metastasis during follow-up. The reported rates of distant metastasis range from 2.4% to 7.5%.[9,15,24]

Eight of 11 patients who developed local recurrence were also found to have distant metastasis, mostly in the lungs. Thus, we suggest that it is critical to reduce local recurrence to prevent distant metastasis.

There are some limitations to this study. As the information was collected retrospectively, this study is liable to selection bias. In addition, as our institute is a tertiary care center, many patients with malignant phyllodes were referred for definitive surgery and radiotherapy, thus influencing the proportion of malignant to benign phyllodes tumors. Moreover, the sample size was small and follow-up duration was relatively short, which may have led to the study being underpowered, thus preventing us from clarifying the role of other prognostic factors to guide the use of adjuvant radiotherapy.

Conclusion

Phyllodes tumor of the breast comprises a heterogeneous group of tumors with unpredictable outcomes. Surgical resection (breast conserving surgery/mastectomy) is the primary modality of treatment for all histological subtypes. The size of the tumor dictates the choice of surgery, as shown in this study. Benign phyllodes tumor portends an excellent prognosis with margin-negative surgical resection. The

Figure 3: Giant phyllodes tumor of breast

addition of radiotherapy postoperatively in the patients with borderline and malignant phyllodes tumors reduced the rate of local recurrence irrespective of margin status. Our experience supports the use of adjuvant radiotherapy in patients with borderline and malignant phyllodes tumors irrespective of margin status.

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Conflicts of interest

There are no conflicts of interest.

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