Evaluation of Phyllodes Tumor of Breast - A Retrospective Study

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Abstract:
Background: Phyllodes tumours are typically large fast growing masses that form from the periductal stromal cell of the breast. The patients typically present with a firm, palpable, rapidly growing mass. This is a retrospective study of clinical experience regarding management of phyllodes tumour both benign and malignant. **Method:** This is a personal study of 28 patients who were studied retrospectively in a time span of June 2011 to February 2018. **Result:** All of these patients were histologicaly diagnosed cases of different varieties of phyllodes tumours (benign 17, borderline 8, malignant 3). Patients were evaluated in relation to their degree of different categories and different modalities of treatment given. All patients were followed up for 2 years of time after treatment. **Conclusion:** Phyllodes tumour are rare fibroepithelial lesion of breast. Accurate preoperative diagnosis is mandatory for correct surgical planning and avoidance of reoperation. Recommended operative technique is wide excision with at least 1 cm of normal margin to avoid recurrence for both benign and malignant tumours.

Indexing words: Phyllodes tumour, Surgical margin, Fibro adeonoma, Malignant phyllodes

Introduction:
Phyllodes tumour is a relatively uncommon benign fibroepithelial lesion of the breast which accounts for <1% (0.3-0.9%) of all breast neoplasm.[1] Most commonly found women between 40-50 years[2] of age.
Chelius described this tumour first in 1827. Johannes Muller (1838) was the first person to use the term cystosarcoma phyllodes. It was believed to be benign until 1943, when Cooper and Ackerman reported on the biological potential of this tumour. In 1981 the World Health Organization adopted the term phyllodes tumour and as describe by Rosen subclassified them as histologically benign, borderline and malignant according to the features such as tumour margins, stromal overgrowth, tumour necrosis, cellular atypia and number of mitosis per high power field.[3-6]

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Most common grade of phyllodes tumour is benign (60-75%) of the cases.[7] phyllodes tumour represents a wide range of clinical and pathological behaviour, so should be regarded as a spectrum of fibroepithelial neoplasm rather than a single disease entity. Histologically these tumuors are characterized by presence of an epithelial component with stromal components which differentiates it from other stromal sarcomas. It is characterized by long clefts and myxoid cellular stroma.[8-10] Preoperative accurate tissue diagnosis is required to avoid reoperation. Malignant phyllodes tumour if inadequately treated can show rapid growth and metastatic spread, while phyllodes tumour which are benign on clinical, radiological and cytological examination are often indistinguishable from fibroadenomas and can be cured by local surgery. So as the nonoperative management of fibroadenomas is widely adopted, the importance of phyllodes tumour today is based on the need to differentiate them from other benign breast lesions. Treatment wide local excision (free margin at least 1 cm) or mastectomy provided histologically clear specimen margin are ensured.[11-13]

In this study patient characteristic, findings on imaging, histopathological diagnosis, evaluation and outcome of surgical treatment given and risk factors associated with recurrence are assessed.

Methods:

This is a retrospective study of 28 patients who were diagnosed case of Phyllodes tumour and underwent surgical management in Rangpur Medical College & Hospital Surgery Department in a time frame of June-2011 to February-2018. The data were collected from hospital registry, analyzed retrospectively regarding physical examination of the patient including age, menopausal status, location and size of the tumour. Investigation reports reviewed including breast imaging (USG and Mammography), histopathological reports. Data regarding therapeutic intervention are also analyzed. Different operative procedures were performed including excision, wide excision, mastectomy, excision followed by mastectomy. Patients are classified into benign, boderline and malignant tumour according to WHO guideline after final histopathological diagnosis. All of the patients were followed up for 2 years after operation for detection of any recurrence.

Result:

We included 28 patients of phyllodes tumour among which 20 patients were premenopausal and 8 were post menopausal. Age range of the pratients was 30 to 55 years and the average age was 39 years of whom 23 patients came with tumour in right breast and remaining patients had tumour in left breast .Lumps were found in upper and outer quadrant in 15 patients, 4 in upper and inner quadrant, 5 patients had centrally locating lump,3 in lower and outer and 1 in lower and inner quadrant. Among 28 patients, 17 patients had benign phyllodes tumour of 3-4 cm in diameter, 8 patients with boderline phyllodes of 5-5.5cm diameter and rest of the patients (3 in number) were found with a malignant phyllodes tumour of 6.5 to 7 cm diameter. The skin changes were observed in the form of dialated veins and blue discoloration in larger tumours with 6-7 cm diameter in 11 patients, but there was no history of nipple retraction of any of them. Two patients with malignant phyllodes and 1 patient of borderline phyllodes found with skin fixity. None of the patients had pectoralis muscle fixation. Clinically palpable axillary lymph nodes were present in 4 patients (11.4%).

Table 1 Details of tumor

Parameter	Benign	Borderline	Malignant
Age			
<40 years	11	2	0
≥40 years	6	6	3
Site			
Right	13	7	3
Left	4	1	0
Quadrant			
UOQ	10	3	2
UIQ	2	1	1
Central	2	3	0
LOQ	2	1	0
LIQ	1	0	0
Operation Type			
Wide Excision	17	8	0
Mastectomy	0	0	3
Operation done for local recurrence			
Wide Excision	2	1	0
Mastectomy	0	0	0
Surgical free margin			
Free >1cm	15	7	3
Positive margin	2	1	0
Tumour size			
3-4 cm	17	0	0
5-5.5 cm	0	8	0
6.5-7 cm	0	0	3
Recurrence (Within 2 years of primary treatment)			
Yes	2	1	0
No	15	7	3

[N.B: UOQ= Upper Outer Quadrant, UIQ= Upper Inner Quadrant, LOQ= Lower Outer Quadrant, LIQ= Lower Inner Quadrant]

Radiological Investigations:

Ultrasonography was used to evaluate 11 cases and mammogram was done in remaining patients.

USG Findings:

On USG tumours were lobulated or rounded or oval with a well circumscribed smooth margin which often shows smooth contours with low level of homogenous internal echoes and the absence of posterior acoustic enhancement. In a predominantly solid mass, fluid filled clefts were highly suggestive of phyllodes tumour.

Mammography Findings:

In this study tumours were found on mammography as well defined mass lesion with a smooth and sometimes lobulated border, a radiolucent halo may be seen around the lesion

due to the compression of the surrounding breast stroma. Coarse microcalcification reported to be found both in fibroadenomas and phyllodes but malignant microcalcification is rare. But USG and mammography could not differentiate between benign and malignant phyllodes tumour on the basis of any definite radiological criteria. Core cut biopsy was performed for preoperative histopathological diagnosis. Which revealed 17 patients with benign phyllodes, 8 had equivocal or indeterminate report, 4 patients had fibroadenoma and remaining 3 patients had malignant phyllodes tumour.

Management:

In our personal series with a preoperative Core cut needle biopsy diagnosis of benign phyllodes tumour of 17 patients we performed wide excision with ≥1cm margin. Patients with indeterminate histology who were 8 in number underwent wide excisional biopsy. The remaining 3 patients with malignant phyllodes underwent mastectomy without any axillary staging. According to the final histopathological report, 17 patients with preoperative diagnosis of benign phyllodes tumour, 11 patients had the same histology and 6 patients had borderline phyllode. Among 8 patients with indeterminate histopathology, 2 patients had borderline phyllodes tumour and 6 patients' benign phyllodes. The remaining 3 patients had malignant phyllodes in final histopathological report. Margin clearance achieved in first operation in 25 patients and in remaining 3 patients we didn't achieve surgical free margin of at least 1 cm from the tumour. Among 28 patients, 3 patients were with malignant phyllodes tumour and we performed simple mastectomy over there. In remaining 25 patients, 17 patients had benign Phyllodes and 8 had borderline tumour. All of our 3 patients in which margins clearance was not achieve, developed local recurrence without any evidence of distant metastases. Among them 2 patients had benign Phyllodes and 1 patient had borderline tumour and the histopathologicl types were same as the primary tumour. All of those patients developed recurrence within 1-2 years follow up period, we performed reexcision in all of these cases with a view to achieve ≥ 1cm tumour free margin. We achieved tumour free margin in all of the cases and we followed up these patients for another 2 years. None of those patients developed any further recurrence.

Table 2 Rading of tumor

Tumour Grade	Size (cm)	Initial Method	≥ 1cm margin clearance	Number of recurrence (within 2 years of primary treatment)	Method of recurrence
Benign	3-4	WLE	15	2	WLE
Borderline	5-5.5	WLE	7	1	WLE
Malignant	6.5-7	Simple mastectomy	3	0	0

[N.B: WLE = Wide Local Excision]

Discussion:

Phyllodes tumour is a relatively uncommon benign fibroepithelial lesion of breast accunts for<1% (0.3-0.9%) of all breast neoplasm that most commonly found in women between 40-50 years.[1-2] In our study, the age range is 30-55 years and the average age 39 years with a time span June 2011 to February 2018. All of the patients presented with breast lump of which 14 patients had rapidly growing lump and 6 had pain in the side of the lump. On USG the tumour were lobulated or rounded or oval with a well circumscribed smooth margins with a low level homogenous internal echoes and on mammography, there were well circumscribed oval or lobulated mass with rounded border.[14-17]

In our series by imaging characteristics we were unable to distinguish fibroadeonoma from phyllodes tumour. According to the international literature, the average size of the fibroadeonoma 2cm where as phyllodes tumour size range in between 4-7 cm.[18] In our personal series the average size for phyllodes tumour was 3.5 cm for benign, 5 cm for borderline and 6.5 cm for malignant phyllodes. Surgical management is the mainstay of treatment. If diagnosed preoperatively, tumour should be resected with atleast 1 cm margins, specifically in the borderline and malignant phyllodes tumours and in case of benign phyllodes, that diagnosed after local excision, of what appeared to be a fibroadeonoma, the approach should be "watch and wait" policy. But as in case of giant phyllodes, an excision with the required margin is often impossible, mastectomy should reserved for larger tumours and should considered in recurrent tumours specially for the malignant histotype.[19,20]

Local recurrence in phyllodes tumour is associated with inadequate local excision and various histological characteristic, including mitotic activity, tumour margin, stromal cellular

atypia. Mastectomy may also be required in tumous of 5-10 cm.[21] As malignant phyllodes mainly spreads by haematogenous route, the proportion of lymph node metastases are <1% (lymph node enlargement in about 10%). That's why routine axillary clearance is no recommended and axillary dissection is needed, when there are histologically positive malignant cells. Chest wall invasion is uncommon.[23]

According to NCCN guidelines wide excision means, excision with a view to obtain surgical margin ≥1 cm narrow surgical margin usually associated with high local recurrence risk but not an absolute indication for mastectomy when partial mastectomy fails to obtain margin of ≥1 cm. Though the role of adjuvant radiotherapy and chemotherapy for soft tissue sarcomas suggest their considerable use in case of malignant phyllodes tumour.[22]

In our personal series we performed wide excision and biopsy with at least 1cm margin clearance in 17 patients, who had preoperative histopathological diagnosis of benign phyllodes tumour, we performed wide excisional biopsy in 8 patients who had preoperative indeterminate histopathological diagnosis. Three patients who had preoperative histopathological diagnosis of malignant phyllodes tumour, underwent mastectomy without axillary staging. We were able to achieve surgical clear margin in 25 patients. Among them 17 patients had benign phyllodes on their final histopathological diagnosis, 8 had borderline phyllodes and 3 had malignant phyllodes. In our series local recurrence occurred within 2 years of follow up in 3 patients. We performed wide excisional biopsy in all of those 3 patients with ≥1 cm margin in all of them and this time we achieved surgical margin clearance. None of those patients developed recurrence in next 2 years of follow up period. If the surgical margin doesn't obtain 1 cm, then further management is different in different classification of phyllodes. Because benign phyllodes tumour should be watched carefully as positive margin in benign has no relation to local recurrence where as in case of borderline and malignant phyllodes, a reexcision or mastectomy should be done to obtain an adequate margin.[18,21,24]

In our study we found that benign phyllodes tumour (2 in no.) recur more than borderline phyllodes (1 in no.). In all of the malignant cases (3 in no.) we didn't find any recurrence and didn't give any radio r chemotherapy as adjuvant treatment for them. Moreover malignant phyllodes are rare cancer of the breast for which surgery is the only effective treatment modality at present. Complete resection with margin clearance appears to be the best method. Inadequate margin clearance associated with local recurrence and conventional chemotherapy and radiotherapy has no effective role.[25]

So according to our study, histopathological type of the phyllodes tumour doesn't correlate to the recurrence because of the very small size, it's difficult to comment on the result. From our data, it's apparent that patients with narrow margin of excision developed recurrence that correlate with many other international literature. A study from the British Columbia Cancer Agency, in July 23rd 2019, analyzed local recurrence rate in 183 patients, where overall 8.7% experienced local recurrence who were followed up for a median of 65 months. With respect to individual sub groups, 5 years outcome for women with benign, borderline and malignant phyllodes were as follows: 6%, 9% & 21% respectively. The 5 years local recurrence rate were 8% for women with negative margins, 6% for those with close margin and 37% for those with positive margins.

In our study we found that the relationship between margin clearance and local recurrence similarly correlate with the international literature. But we were unable to demonstrate a statistically significant correlation between age, race, pain or size of the mass, family H/O breast cancer, H/O OCP, post-menopausal HRT and local recurrence, metastatic disease or death.

In conclusion from our study surgical margin significantly affect the risk of local recurrence for all subtypes of phyllodes tumour.

Conclusion:

Phyllodes tumour is relatively rare tumour of the breast with specific clinical characteristics. Preoperative histopathological diagnosis is very important for proper management of phyllodes tumour and because of their tendency to recur, surgical wide excision (≥1cm normal margin) is necessary and malignant potential of this tumour should also be kept in mind.

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