

A Single Centre Study of Recurrence in Phyllodes Tumour

Ashish Kumar Dubey¹, Sunil Kumar Saxena², Surendra Kumar Padarya³,
Shatkratu Dwivedi⁴

¹Assistant Professor, Department of Surgery, Govt. Bundelkhand Medical College, Sagar
M.P

²Associate Professor, Department of Surgery, Govt. Bundelkhand Medical College, Sagar
M.P

³Assistant Professor, Department of Orthopaedics, Govt. Bundelkhand Medical College,
Sagar M.P

⁴Assistant Professor, Department of Community Medicine, Govt. Bundelkhand Medical
College, Sagar M.P

Received: 15-06-2022 / Revised: 18-07-2022 / Accepted: 30-08-2022

Corresponding author: Dr Shatkratu Dwivedi

Conflict of interest: Nil

Abstract

Background: Rare fibroepithelial neoplasms of the breast include phyllodes tumors. These constitutes less than 1% of all female breast neoplasms., Correct surgical planning and recurrence prevention are made possible by accurate preoperative pathological diagnosis. Treatment could be either lumpectomy or simple mastectomy to achieve histopathological clear margins. Due to the lack of knowledge regarding phyllodes tumors in general and in India in particular, the study's goal included a detailed research analysis of cases and discussion of phyllodes tumour recurrence.

Materials and Methods: This study was a systematic retrospective record-based 3-year review of patient with phyllodes tumour admitted in department of surgery in a tertiary care institute was done from 2018-2021. Records were analyzed and researched with appropriate statistical methods.

Results: Nineteen (19) patients were enrolled in this study. There median age was 45 years., 16 patients were treated by lumpectomy, 2 patients treated by simple mastectomy & 1 patient by modified radical mastectomy i.e. 3 were observed with recurrence.

Conclusion: In present time, early diagnosis and aggressive surgical management is foremost the best treatment for Phyllodes tumour. This will require good reporting, compliance & multicentric studies globally.

Keywords: Phyllodes tumour, Recurrence, lump in breast, Carcinoma, Mastectomy

This is an Open Access article that uses a fund-ing model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Environmental changes, exposure to polluting substances, radiation injury induced by ultraviolet radiation, infrared

radiation and other carcinogenic chemicals including biological hardware are amounting to increase in cancer among the population.

Mutation caused by above mentioned etiopathology are a big threat for development of benign and malignant neoplasm. "Phyllodes tumors are uncommon fibroepithelial neoplasms of the breast. They make up less than 1% of all female breast neoplasms and typically affect women aged 35–55 years [1,2]. & "have incidence of about 2.1 per million [3,4]

"Chelius [5] in 1827 first described this tumor. 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 malignant biological potential of this tumor. In 1981 [6] the World Health Organization adopted the term phyllodes tumor and as described by Rosen [7] subclassified them histologically as benign, borderline, or malignant", as described in Table 1. "In particular, borderline and malignant subtypes exhibit an especially recurrent and metastatic nature, with a reported survival time for patients with malignant phyllodes tumors as low as two years." [8,9]

Table 1: Histological classification of Phyllodes Tumours

Parameters	Benign	Borderline	Malignant
Mitoses/10 HPF	<5	5–9	≥10
Tumour borders	Well defined	Well-defined, may be focally infiltrative	Infiltrative
Stromal atypia	None to mild	Mild to moderate	Marked
Stromal overgrowth	Absent	Absent or very focal	Often present
Stromal cellularity	Cellular, usually mild, may be non-uniform or diffuse	Cellular, usually moderate, may be non-uniform or diffuse	Cellular, usually marked or diffuse
Malignant heterologous stromal elements	Absent	Absent	May be present

In the initial stage it is quite difficult to differentiate a small phyllodes lesions from fibroadenoma of the breast .As also the initial peak of development of fibroadenoma and phyllodes vis-à-vis is same .However there is no second peak in fibroadenoma as compared to phyllodes tumour which has its second peak at the age of 40-45 years .Comparing with malignancy the recent studies shows decrease in the age group that i.e. reduced age group for development of carcinoma of breast and the continuation plateau phase till nearly 65 years of age group.

Females are point of study in this article and we have done a single centre retrospective study of recurrence in the cases of phyllodes

tumour. Since phyllodes tumour are fibroepithelial lesions, most of these lesions are locally malignant which spare the ducts, acini, lobules and other milk producing tissues. Sparing of the milk producing tissue is beneficial since this prevents the neoplasm from becoming malignant.

Because this type of tumour is tip of the iceberg in communities, most hospitals depend on data from small retrospective studies to guide management choices. The objectives of this study were detail study of cases & discussion of recurrence of phyllodes tumour due to the dearth of information about phyllodes tumour in general and in the India in particular.

Materials and Methods

A systematic retrospective record-based review of patient with phyllodes tumour admitted in department of surgery of a tertiary care teaching centre was done with the patient from 2018-2021.

Total number of patients in study period with phyllodes tumour was found to be 19 and all the 19 patients were actively followed, complications occurred in 8 patient's which included development of oedema over the local site, lymphoedema of the arm, wound infection and recurrence of the tumour. Recurrence of phyllodes tumour was observed in 3 patients and the rest patients had minimal complications which

were actively treated and well tolerated by the patients. The 19 patients of phyllodes tumour presented into the outpatient department with the complaints of lump in the breast and slight dragging pain in the affected breast.

Investigation to confirm the pathology were done which included FNAC in all the 19 patients, trucut biopsy in 7 patients and incisional biopsy in 4 patients. Rest investigation included blood investigation which comprised of complete blood count, liver function test, renal function test, immunological status, USG abdomen, x-ray chest PA view. Tumour were classified according to Table 2.

Table 2 : No. of patients according to histological classification

Histological classification	No. of Patients	Percentage
Benign	16	84.2%
Borderline	2	10.5%
Malignant	1	5.3%

“The National Comprehensive Cancer Network and MD Anderson guidelines recommend wide local excision of phyllodes tumour, aiming for margins 1cm or greater (≥ 1 cm).” [11,12] Also, “Smaller margins offer the benefit of improved cosmetic outcomes and reduce the need for further surgery when pathological margins of 1cm or greater are not achieved.” [13] “Surgical excision with negative surgical margins is the mainstay of treatment and is associated with relatively high disease-free survival and long-term survival rates and a low recurrence rate.” [14,15]

Thus, according to the bed head ticket *al* the 19 patients underwent surgery which included Lumpectomy in 15 patients and simple mastectomy in 3 patients and modified radical mastectomy in 1 patient.

“Since phyllodes tumors are locally malignant tumor especially when not excised with a clear margin and very

unpredictable in growth and metastatic activity, it is very necessary to follow up the patient regularly at 6-month interval for the first two years (chances of recurrence are maximum in the first two years) and then on yearly basis.” [16] Hence all the patients were followed up every 15 days for first two months followed by monthly checkup for 6 months and 3 monthly checkups thereafter. In the follow up period, all the patients in every checkup underwent clinical examination, routine blood investigation and ultrasonography of the breast in few selected patients.

Results

Number of patients included in this study were 19, over a period of 3 years starting from January 2018 till December 2021. Of these 19 patients ,5 patients were young females between 16-25 years of age, two patients 26-35 years of age and rest 12

patients were between 36-55 years of age group as shown in Fig 1.

mastectomy was in oldest age group and 3 patients who underwent simple mastectomy were also in the older age group.

Patient who underwent modified radical

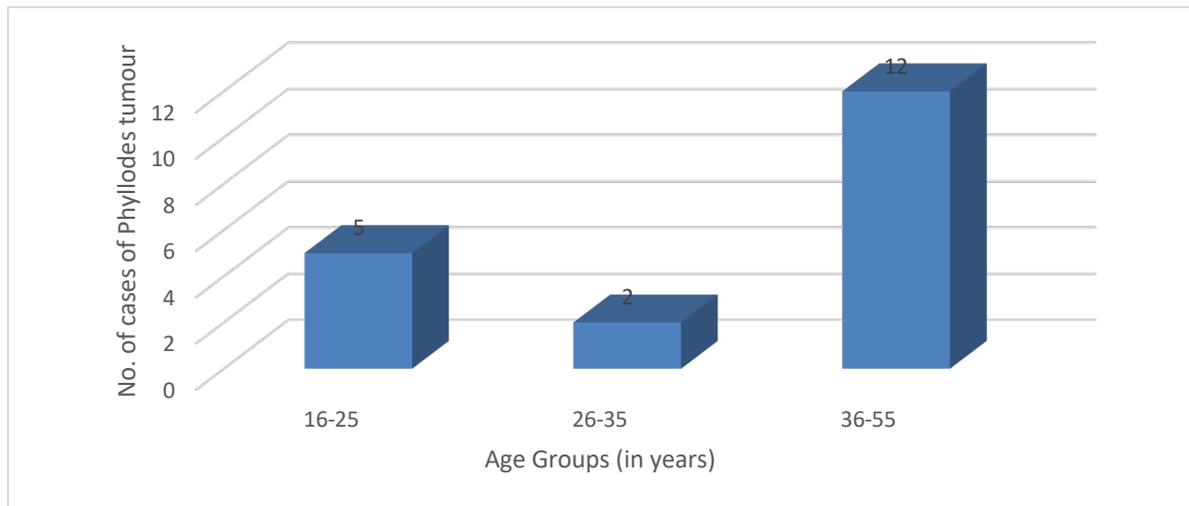


Figure 1: No. of Cases of Phyllodes Tumour

Rest all 15 patients underwent lumpectomy .4 patients who underwent lumpectomy belong to the younger age group 16-25 and 11 patient 26-35 years age group. All the patients who underwent lumpectomy did not have any sequelae in the follow up period of 2 years. Two patients from older age group who underwent modified radical mastectomy and 1 patient from 36-55 years age group who underwent simple mastectomy have recurrence of the disease. Retrospective analysis to know the cause for recurrence was done along with the pathologist specimen and slides were reviewed and was found that the patients who had recurrence had mitotic activity in the peripheral zone of the lump margins of the skin/tumour. It was found that if the margins were negative for any mitotic activity, recurrence was quite uncommon.

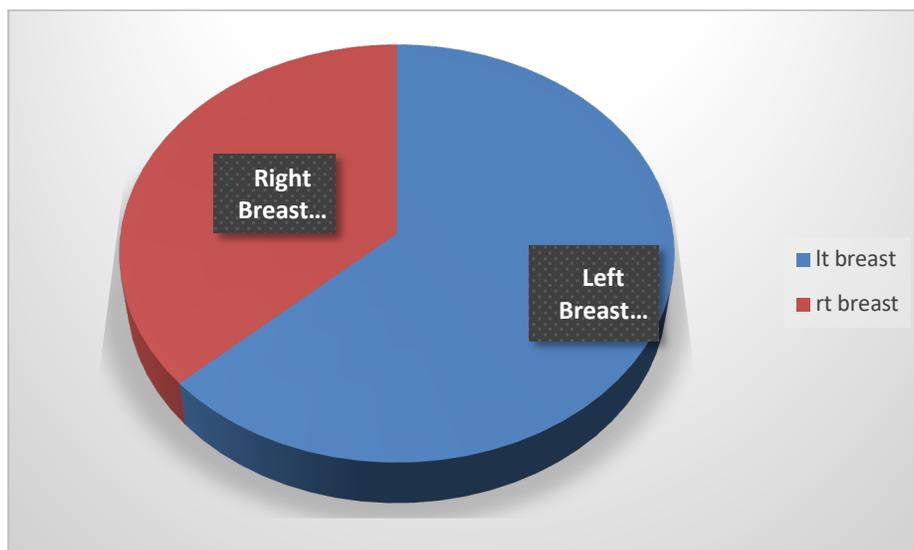


Figure 2: Phyllodes Tumour according to site

Discussion

Regarding phyllodes tumour which has a pattern of leaf like appearance which is also termed as serocystic disease of Brodie is mostly benign in nature and very slow growing and rarely malignant.

Records of is various studies done previously are also suggestive of benign nature of the tumour. Involvement of lymph node of the axilla is very rare except for inflammatory condition which occur due to superadded soft tissue infection of the overlying skin or nipple areola complex.

This inflammatory /reactive lymphadenopathy due to infection of the soft tissue is the result of pressure necrosis and damage to underlying and overlying tissue.

In this study, the patients who presented in early stages without soft tissue complication, did not have any inflammatory lymphadenopathy similar to study by Abe M *et al* who in their study noted that "All these patients underwent lumpectomy with 1 cm. margin excision and tolerated the surgery well and no complications were recorded in 3-year follow-up. The most common site of metastases of PTs is the lung, followed by the bone, heart and liver." [17] But "Because axillary lymph node metastasis occurs in <1% of patients with PT, axillary lymph node dissection is not routinely performed." [18,19]

Few patients who underwent simple mastectomy was because of the involvement of the skin in 2 patients and nipple areola complex in 1 patient.

The 2 patients of simple mastectomy had the necrosis of the skin of the upper outer quadrant and the patients with nipple areola complex had disfigured nipple and areola.

It was nearly mutilated in appearance very difficult to identify the complex hence the decision doing of simple mastectomy in

there 3 patients was taken and the decision was not regretful.

Another patients, an old women of more than 60 years of age with a tissue biopsy of phyllodes tumour had a lymph node in the axilla which were firm and matted but still the cytology report was of inflammatory response .To further add upon the involvement of skin ,the size of the mass and the thrombosis of the peripheral veins at the inferior border of the breast advocated ,the surgical team to take the decision of doing modified radical mastectomy .Thrombosis of the veins at the inferior aspects of the breast ,also made us to consider the possibility of Mondor's disease ,however ,since the modified radical mastectomy was being considered hence no further diagnostic evaluation regards to Mondor's disease was done.

The histopathological report which had the positive margins was of the patients who underwent modified radical mastectomy and later on patients was sent on radiotherapy, in concurrence to other studies "Radiation therapy (RT) is often used because Phyllodes tumour tends to be locally aggressive." [20-22]

Two (2) patients developed local site complications which were seroma formation at the wound site and lymphedema of the arm in the patients of the modified radical mastectomy .Patients who developed oedema and seroma ,were treated by the aspiration of serous fluid and broad spectrum antibiotics coverage ,the patients with lymphedema who underwent modified radical mastectomy was treated with various modalities including non-depending position of the arm ,crape bandaging of the arm and serratiopeptidase in extended doses and slight physiotherapy patient responded well and later on received radiotherapy and doing well till last follow up.

This study of 3 years duration with sample size of 19 patients has revealed few facts which we would like to discuss.

Of the 19 patients available in the records with the phyllodes tumour disease, reveals the fact that the presence of cystosarcoma phyllodes is much more in the population then reported in the literature.

Secondarily what we found was that phyllodes tumour was mostly found in patients with low socioeconomic status contrary to the carcinoma which is reported in good socioeconomic strata. However, this point should undergo more authentic reporting since underreporting of breast carcinoma is also a major setback in actual incidence of carcinoma breast

The patients of cystosarcoma phyllodes in this study were from all the age ranges with more deviation towards younger age group, suggesting the possibility of hormonal imbalance as a factor for development of this benign tumour, however this also requires evaluation and research at the molecular level.

Any correlation with menarche or early or late pregnancy could not be established with this study may be owing to small sample size and small duration with of study, we would like to suggest that if co-relation of pregnancy and menarche, could be established we might be able to reduce the incidence of this benign disease.

Further all early diagnosis and early aggressive and planned surgical excision with negative margins is the best treatment for this disease because we noticed recurrence and dysplastic changes, towards malignancy in the patients with long duration of in vivo disease. According to Samuel Ogunbiyi *et al.* "A negative margin is acceptable treatment following a lumpectomy for Phyllodes tumors. Only patients with a positive margin should undergo a revision." [23]

Conclusion

Thus, from this retrospective study of 3 years duration has revealed few facts and raises of battery of questionnaire which requires detailed study and research.

Early diagnosis and aggressive surgical treatment are far most the best treatment without any controversy. However, if we could correlate menarche, puberty, and pregnancy with the development of this disease, we could possibly control the incidence of this tumour, however this will require good reporting, very large sample size and multicentric study globally.

The incidence of phyllodes tumour which is being reported is the tip of iceberg and why vast majority of the patients with this disease are neglected or underreported. Might be because of benign nature these patients get operated or treated at small centre without notification.

We would like to suggest development of central, monitoring/reporting system for the benefit of patients and research.

References

1. Zhou ZR, Wang CC, Yang ZZ *et al.* Phyllodes tumors of the breast: diagnosis, treatment and prognostic factors related to recurrence. *J Thorac Dis* 2016; 8: 3,361–3,368.
2. Guillot E, Couturaud B, Reyat F *et al.* Management of phyllodes breast tumors. *Breast J* 2011; 17: 129–137
3. B. Salvadori, F. Cusumano, R. Del Bo *et al.*, Surgical treatment of phyllodes tumors of the breast, *Cancer*, 1989;63(12):2532–2536.
4. L. Bernstein, D. Deapen, and R. K. Ross, The descriptive epidemiology of malignant cystosarcoma phyllodes tumors of the breast, *Cancer*, 1993; 71(10):3020–3024.
5. M. Chelius, *Neue Jahrbucher Der Teutschen Medicin and Chirurgie*,

- Naegele und Puchelt, Heidelberg, Germany, 1827
6. World Health Organization, Histologic Typing of Breast Tumors, vol. 2, WHO, Geneva, Switzerland, 2nd edition, 1981.
 7. P. P. Rosen, Rosen's Breast Pathology, Lippincott William Wikins, New York, NY, USA, 2nd edition, 2001.
 8. Mitus JW, Blechartz P, Walasek T et al. Treatment of patients with distant metastases from phyllodes tumor of the breast. *World J Surg* 2016; 40(2): 323–328.
 9. Ben Hassouna J, Damak T, Gamoudi A et al. Phyllodes tumors of the breast: a case series of 106 patients. *Am J Surg* 2006; 192(2): 141–147.
 10. Lakhani SR, Ellis IO, Schnitt SJ, Tan PH, van de Vijver MJ (eds.) WHO Classification of Tumours of the Breast, 4th ed. Geneva: World Health Organization; 2012
 11. National Comprehensive Cancer Network. Breast Cancer. Clinical Practice Guidelines in Oncology (NCCN Guidelines). Plymouth Meeting, PA: NCCN; 2019
 12. MD Anderson Cancer Center. Phyllodes Tumor. Houston, TX: University of Texas MD Anderson Cancer Center; 2019. <https://www.mdanderson.org/content/dam/mdanderson/documents/for-physicians/algorithms/cancer-treatment/ca-treatment-phyllodes-web-algorithm.pdf> (cited June 2022)
 13. A Thind et al. Surgical margins for borderline and malignant phyllodes tumours. *Ann R Coll Surg Engl* 2020; 102: 165–173.
 14. Pandey M, Mathew A, Abraham EK, et al. Primary sarcoma of the breast. *J Surg Oncol* 2004; 87: 121–125
 15. Fou A, Schnabel FR, Hamele-Bena D, et al. Long-term outcomes of malignant phyllodes tumors patients: an institutional experience. *Am J Surg* 2006; 192: 492–495
 16. Shashi Prakash Mishra et al. Phyllodes Tumor of Breast: A Review Article. *ISRN Surgery* Volume 2013, Article ID 361469, 1-10.
 17. Abe M, Miyata S, Nishimura S, et al. Malignant transformation of breast fibroadenoma to malignant phyllodes tumor: long-term outcome of 36 malignant phyllodes tumors. *Breast Cancer* 2011; 18: 268–272.
 18. Salvadori B, Cusumano F, Bo RD, et al. Surgical treatment of phyllodes tumors of the breast. *Cancer* 1989; 63: 2532–2536
 19. Chen WH, Cheng SP, Tzen CY, et al. Surgical treatment of phyllodes tumors of the breast: retrospective review of 172 cases. *J Surg Oncol* 2005; 91: 185–194.
 20. Pandey M, Mathew A, Kattoor J, et al. Malignant phyllodes tumor. *Breast J* 2001;7: 411–416.
 21. Barth RJ Jr, Wells WA, Mitchell SE, et al. A prospective, multi-institutional study of adjuvant radiotherapy after resection of malignant phyllodes tumors. *Ann Surg Oncol* 2009; 16: 2288–2294.
 22. Gnerlich JL, Williams RT, Yao K, et al. Utilization of radiotherapy for malignant phyllodes tumors: analysis of the National Cancer Data Base, 1998–2009. *Ann Surg Oncol* 2014; 21: 1222–1230.
 23. Samuel Ogunbiyi et al. Phyllodes tumour of the breast and margins: How much is enough? *Can J Surg*, Vol. 62, No. 1, February 2019.E19-E21.