Section: Pathology

Original Research Article

PHYLLODES TUMOUR OF THE BREAST: A CLINICOPATHOLOGICAL STUDY IN A TERTIARY CARE HOSPITAL IN GARHWAL REGION

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Abstract

Background: Phyllodes tumour is a rare fibroepithelial tumour which comprises of less than 1% of all breast tumours. This tumour has been divided into benign, borderline and malignant variants based on the histological features. **Aim:** The study was undertaken with the aim to analyze and interpret the clinicopathological features of phyllodes tumour which presented in our hospital in this hilly region. Also there has been very little study, if any, carried out on phyllodes tumour in our region. **Material And Methods:** A retrospective study, over a period of 10-years, was carried out on the material, which included the histopathological slides and tissue blocks of phyllodes tumour. The relevant clinical data related to these was obtained from the archives of department of Pathology. **Results:** In this retrospective study, a total of 22 cases of phyllodes tumour were found, out of which 18(81.8%) were benign, 2(9.1%) were borderline and 2(9.1%) were malignant. It was seen in a wide age group ranging from 19 to 70 years and the mean size of tumour at presentation was 6.22 cms. Benign phyllodes tumour was the most common variant seen in our study. **Conclusion:** Phyllodes tumor shows a wide spectrum of histomorphology. Though there are no clearly distinct boundaries between the three histological grades of phyllodes tumour yet the grading system is the best guide for treatment protocol and clinical outcome.

INTRODUCTION

Breast cancer is one of the most common human neoplasms, accounting for approximately one-quarter of all cancers in females worldwide and 27% of cancers in developed countries with a Western lifestyle.[1] Phyllodes tumour of the breast is a rare fibroepithelial tumour that constitutes less than 1 percent of all breast tumours. Phyllodes tumors of the breast are biphasic fibroepithelial neoplasms analogous to fibroadenomas.[2] Phyllodes tumours are characterized by a double layered epithelial component surrounded by a hypercellular mesenchymal component, typically presenting in leaf-like processes.[3] Phyllodes tumour have been described as early as 1774, when they were known as a giant type of fibroadenoma ,but the lesion was first fully characterized in 1838 by Johannes Muller and introduced the tumours as cystosarcoma phyllodes.[4] Despite of sarcoma-term in their name, they were believed to be benign initially, however, in 1931 Lee and Park reported the first case of metastatic phyllodes tumour.[5] World Health Organization (WHO) started to use the term phyllodes tumour in 1981[6] Phyllodes tumor presents a morphologic continuum from benign to malignant and based on histologic features of nuclear atypia, stromal cellularity, mitotic activity, tumor margin appearance, and stromal overgrowth, the World Health Organization classifies phyllodes tumors into benign, borderline, and malignant phyllodes tumour (3) as depicted in table 1. The diagnosis of phyllodes tumour is purely based on histological features, but in the absence of clear defining boundaries for each of these histologic parameters, and interobserver variability, reliable classification is challenging.

MATERIALS AND METHODS

This was a hospital-based retrospective observational study carried out in the Department of Pathology, Veer Chander Singh Garhwali Government Medical Science and Research Institute, Srinagar, Garhwal, Uttarakhand. The materials for the study included histopathology

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slides, and tissue blocks, of all phyllodes tumour specimens received between Jan 2010 to Dec 2021. All cases of phyllodes tumor diagnosed on histopathology were taken for study. The hematoxylin and eosin (HandE) stained histopathology slides were retrieved and were reviewed using light microscopy, under various magnifications. Fresh sections were taken from tissue blocks in some cases, wherever required, and were stained with (HandE) stain. All the clinical, investigational, operative, pathological details were collected from archival file records. There were a total of 22 cases of phyllodes tumour, out of which 18 were benign, 2 borderline and 2 malignant. Classification into benign, borderline, and malignant categories relied on the histological features of degree of stromal hypercellularity, cytologic atypia, mitotic activity, stromal overgrowth, and nature of the borders (circumscribed vs permeative). Stromal hypercellularity and cytologic atypia were categorized as mild, moderate, or severe. Stromal mitotic activity was quantified per 10 high-power fields (hpf) of the microscope objective (40× objective and 10× eyepiece) in the most mitotically active areas of the stroma. Stromal overgrowth, defined as a low-power field (4× microscope objective and 10× eyepiece) that comprised only stroma without epithelial elements, was deemed absent or present.[7] The various histopathological features of all cases were noted down. Data were analyzed using tables, figures, and percentages.

RESULTS

A total of 22 cases were diagnosed as phyllodes tumour during the study period and among all those cases, 18 (81.8%) were benign, 2 (9.1%) were borderline, and 2 (9.1%) were malignant. All the patients were women and the age of the patients ranged from 19 to 70 years, with a mean of 41. 81 and a median of 43. The tumor size ranged from 2 to 14 cm with a mean of 6.22 cms. Among all tumours, 11 (50%) were less than or equal to 5 cm and 11 (50%) were more than 5 cm size in their greatest dimension. The size of benign phyllodes tumour ranged from 2 to 10 cms while all borderline and malignant phyllodes tumours were greater than 8 cms. All patients presented with single palpable lump in the breast. 2 patients had ulcers overlying the lump. Axillary lymphadenopathy was noted in 3 cases and all of these lymph nodes were showing reactive lymphoid hyperplasia. The right sided breast were affected in 12 (54.54%) and left sided breasts were affected in 10 (45.46%) cases. None of the patients in our study had bilateral tumors. Macroscopically 17 tumors (77.27%) were well circumscribed and 5 (22.73%) was poorly circumscribed. Necrosis was noted in 3 tumors (13.63%) and was not evident in rest of cases. Hemorrhage was appreciated in 3 tumors (13.63%) and was absent in rest of the cases. The number of microscopic slides reviewed for each case ranged from 1 to 14 (mean 5). Leafy frond like structures characteristic of phyllodes tumor were observed in atleast some parts of the tumor in most of the cases (fig.1). Mitotic activity of all the tumours ranged from 0 to 14 mitoses per 10 hpf (mean, 2.27/10 hpf) (fig.2). Malignant variants showed the maximum mitotic activity with a mean of 13mitosis/hpf followed by borderline variants which showed a mean of 6.5 mitosis/hpf. (table 2) Stromal multinucleated giant cells were seen across all of these variants and were seen maximum in malignant variant with a mean of 3/10hpf. Myxoid degeneration was observed in 7 cases (31.82%) while 15(68.18%) cases didn't have any myxoid degeneration. Hemorrhage was observed in 5 lesions (22.72%) while the rest of cases didn't have any. In 3 cases (13.63%) tumor necrosis was present. Stromal metaplasia was observed in 2 cases (9.09%) which included benign adipose (1 case) and chondromyxoid (1 case) metaplasia. Hyperplasia of the epithelial elements of the phyllodes tumor was observed in 6 cases(27.27%) while no case had any malignant epithelial lesion (fig.3). None of the patient in our study showed any metastasis though 2 patients did have reactive lymphoid hyperplasia of lymph nodes.

Table 1: Three-tiered grading system for phyllodes tumour based on 2012 World health organization classification

Criteria	Benign	Borderline	Malignant
Stromal cellularity	Minimal	Moderate	Marked
Stromal atypia	Minimal	Moderate	Marked
Stromal overgrowth	Minimal	Moderate	Marked
Mitosis/10 high power fields	0-4	5-9	≥10
Tumour margins	Well circumscribed with pushing tumour margins	Zone of microscopic invasion around tumour margins	Infiltrative tumour margins

Table 2: Clinicopathological features of phyllodes tumour

Diagnosis	Number of cases(%age)	Mean age(years)	mean tumour size(cms)	Mean mitosis/10hpf	Mean number of smngc/10hpf	Metastasis
Benign PT	18(81.82%)	40.55	5.16	1.94	1.05	0
Borderline PT	2(9.09%)	51.5	10	6.5	2.5	0
Malignant PT	2(9.09%)	43.5	12	13	3.0	0

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hpf: high power field
smngc: stromal multinucleate giant cell

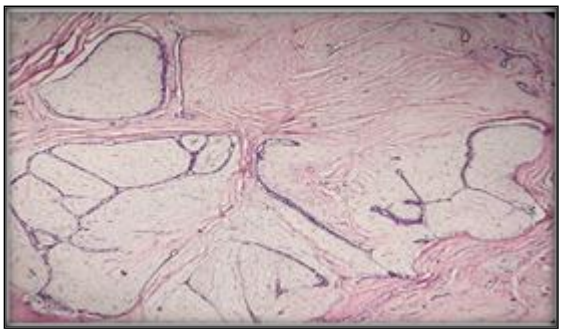

Figure 1: Showing scanner view of benign phyllodes tumour showing leaf like processes.(HandE stain 100X)

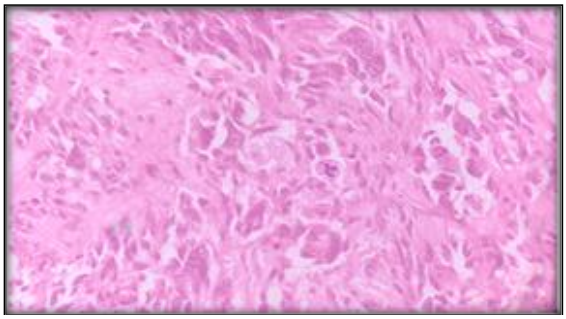

Figure 2: Photomicrograph showing mitotic figures and pleomorphism of stromal cells.(HandE stain 400X)

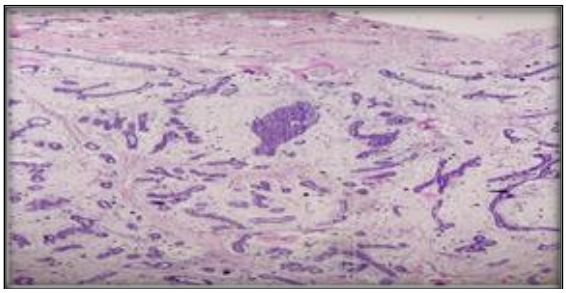

Figure 3: Photomicrograph showing focal epithelial hyperplasia .(HandE stain 100X)

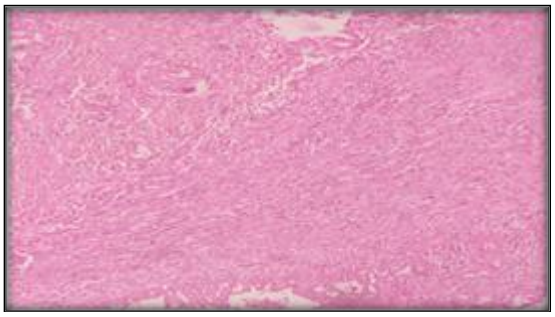

Figure 4: Photomicrograph showing stromal overgrowth, hypercellularity and nuclear pleomorphism.(HandE stain 100X)

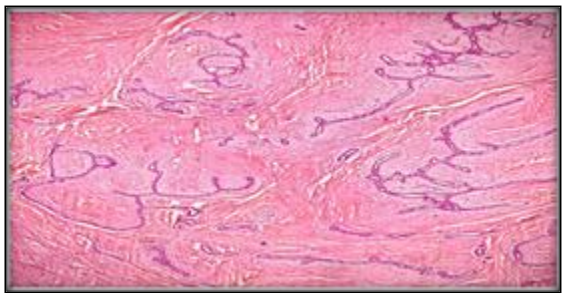

Figure 5: Photomicrograph showing peritubular stromal proliferation .(HandE stain 100X)

DISCUSSION

Phyllodes tumour of the breast has been a challenge due to its unpredictable clinical presentation, uncertain pathological behavior, and inaccurate preoperative diagnosis. Its unpredictable clinical course and high recurrence rate makes it unique from other breast diseases, which leads to dilemma for treatment plan.[2] Histopathologically, phyllodes tumour is composed of stromal and epithelial tissue components and it is the stromal component (fig 4) which predominantly determines the aggressive behavior of this tumor, though other variations of the epithelial component may also be encountered. Classification of this tumour, according to WHOs criteria, into benign, borderline and malignant has been widely accepted and taken into account. This classification is still far from ideal as there is difficulty in distinguishing it from fibroadenoma and no clear cut subdivision into the 3 recognized grades of phyllodes tumors.

In our study the median age of presentation of phyllodes tumour was 43 years which is slightly less than the median age in study of Reinfuss *et al.* and Salvadori *et al.*[8,9] and almost at par with study of Naranakar *et al.*[2] The incidence of different histological variants reported varies in different studies and the incidence of different histological variants in our study came out as; benign 81.8%, borderline as 9.1% and malignant as 9.1%. The various studies have been showing incidence of benign phyllodes between 35–64% while for malignant tumors it is about 25%.[10,8.11] The incidence of malignant variant of phyllodes tumour came out to be the least as compared to other studies. Malignant and borderline tumours were comparatively bigger in size as compared to benign variants. Axillary lymphadenopathy was found to be in 3 (13.63%) cases which happens to be at par with study of Narayankar *et al.*[2] but much lesser as compared to studies of Bhargav *et al.* and Chen *et al.*[12,13] who reported it as high as 20–25%. All the cases of lymphadenopathy in our study came out to be due to reactive lymphadenopathy. No metastatic axillary lymph nodes were found in our

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series, and it has been reported as <1% in most of the studies.[12,13] Epithelial hyperplasia was seen associated with 27.27% cases of phyllodes tumour which is quite paradox to study of Tan P H *et al.*,[14] which found out epithelial hyperplasia associated with 74% of cases. Average mitotic activity was least in our study as compared to most of the other studies as percentage of malignant phyllodes tumour was the least. There has been quite a variability in interpretation and cutoffs of the parameters used for histological classification of the phyllodes tumour. Kleer *et al.*[15] in their study have considered benign phyllodes tumour as those having fewer than 1 mitosis/hpf, while as Rosen[16] considered mitosis less than 2 mitosis/hpf as criteria for benign phyllodes tumour. Moffat *et al.*[17] went a step higher and regarded having mitotic figures less than 10/hpf as a criteria for benign variant. In our study we have taken a cut off criteria of upto 4 mitotic figures/hpf for benign phyllodes tumour, 5-9 mitotic figures /hpf for borderline and 10 or more/hpf for malignant phyllodes tumour which is in accordance to WHOs classification. This variability should be addressed and diagnosis should be made as per a standard protocol in order to overcome the interobserver variability in making the diagnosis. Also grading of atypia is subjected to interobserver inconsistency. The recognised clinical pertinence of grading phyllodes tumours histopathologically is to predict clinical behavior: benign tumours have the potential to locally recur; borderline tumours have the potential to recur locally, and have a very low risk of metastasis; and malignant tumours have the highest risk of metastatic behavior, which may eventually prove fatal. Also the mode of treatment is different for these three variants.

CONCLUSION

Phyllodes tumour is one of the very rare group of tumours. The histological classification of phyllodes tumour has been a very important way of predicting the clinical outcome and an important guide for treatment application. Many studies have been showing that the histological features correlate well with the prognosis and as such histological grading of phyllodes tumour is of utmost significance. In our series of patients, benign phyllodes tumour was the most common variant of the phyllodes tumour which is in accordance with most of the studies worldwide, though the percentages of benign variant was considerably more in our region. Furthermore, from our study, we concluded that while diagnosing phyllodes tumour, various histological features according to WHOs criteria should be thoroughly kept in mind for making correct diagnosis and to minimize interobserver bias.

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Conflicts of interest

The authors declared that they have no conflict of interests.

REFEREMCES

1. Makki J. Diversity of Breast Carcinoma: Histological Subtypes and Clinical Relevance. Clinical Medicine Insights: Pathology 2015:8 23–31.
2. Narayanakar RP, Gangaiah DM, Althaf S, Dev K, Kurpad V, Gurawalia J. Cystosarcoma phyllodes: Pathological enigma: A retrospective review of 162 cases. Indian J Cancer 2015;52:365-8.
3. The World Health Organization. The World Health Organization histological typing of breast tumors – Second edition. The World Organization. Am J Clin Pathol 1982;78:806-916.
4. Fiks A. Cystosarcoma phyllodes of the mammary gland—Muller's tumor. For the 180th birthday of Johannes Muller. Virchows Arch A Pathol Anat Histol 1981;392:1–6.
5. Lee B, Pack G. Giant intracanalicular broadenomyxoma of the breast. The so-called cystosarcoma phyllodes mammae of Johannes Muller. Am J Can. 1931;93:250-68.
6. World Health Organization. Histological typing of breast tumours. 2nd edition. Vol 2. Geneva, Switzerland: WHO;1981.
7. Ward RM, Evans HL. Cystosarcoma phyllodes: a clinicopathologic study of 26 cases. Cancer. 1986;58:2282- 2289.
8. Reinfuss M, Mitus J, Duda K, Stelmach A, Rys J, Smolak K. The treatment and prognosis of patients with phyllodes tumor of the breast: An analysis of 170 cases. Cancer 1996;77:910-6.
9. Salvadori B, Cusumano F, Del Bo R, *et al.* Surgical treatment of phyllodes tumors of the breast. Cancer 1989;63:2532-6.
10. Ben Hassouna J, Damak T, Gamoudi A, *et al.* Phyllodes tumors of the breast: A case series of 106 patients. Am J Surg 2006;192:141-7.
11. Macdonald OK, Lee CM, Tward JD, Chappel CD, Gaffney DK. Malignant phyllodes tumor of the female breast: Association of primary therapy with cause-specific survival from the surveillance, epidemiology, and end results (SEER) program. Cancer 2006;107:2127-33.
12. Bhargav PR, Mishra A, Agarwal G, Agarwal A, Verma AK, Mishra SK. Phyllodes tumour of the breast: Clinicopathological analysis of recurrent vs. non-recurrent cases. Asian J Surg 2009;32:224-8.
13. 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;91:185-94
14. Tan PH, Jayabaskar T, Chuah KL, *et al.* Phyllodes tumour of the breast: the role of pathological parameters, Am J Clin Pathol 2005;123:529-540.
15. Kleer CG, Giordano TJ, Braun T, *et al.* Pathologic, immunohistochemical, and molecular features of benign and malignant phyllodes tumors of the breast. *Mod Pathol.* 2001;14:185-190.
16. Rosen PP. Fibroepithelial neoplasms. In: *Rosen's Breast Pathology.* 2nd ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2001:163-200.
17. Moffat CJC, Pinder SE, Dixon AR, *et al.* Phyllodes tumours of the breast: a clinicopathological review of thirty-two cases. Histopathol. 1995;27:205-218.

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