REVIEW ARTICLE

Unfolding the Leaf: A Comprehensive Insight into Phyllodes Tumors of the Breast: A Review Article

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ABSTRACT

Phyllodes tumors (PTs) are uncommon fibroepithelial lesions of the breast that comprise <1% of all breast neoplasms. These tumors are characterized by a distinctive histological pattern resembling a "leaf-like" architecture, arising from a biphasic proliferation of stromal and epithelial components. PTs are classified into benign, borderline, and malignant subtypes based on histological features, such as stromal cellularity, atypia, mitotic activity, tumor margins, and stromal overgrowth. While the majority is benign, all variants have the potential for local recurrence and, in the case of malignant types, distant metastasis. Their clinical and radiologic presentation often overlaps with fibroadenomas, making accurate pre-operative diagnosis challenging. The etiology of PTs remains poorly understood, although genetic mutations and hormonal influences are suspected to contribute. Surgical excision with wide margins remains the cornerstone of treatment, as incomplete resection is associated with a higher risk of recurrence. The role of adjuvant radiotherapy and chemotherapy remains limited and is generally reserved for high-risk or recurrent malignant cases. Prognosis depends primarily on histological classification, surgical margins, and the presence or absence of metastasis. This review provides a comprehensive overview of the present knowledge surrounding the epidemiology, pathogenesis, histopathology, classification, and management of PTs. Emphasis is placed on the importance of accurate diagnosis and appropriate surgical planning to reduce recurrence risk. In addition, the article explores evolving clinical guidelines and highlights areas requiring further research, aiming to support evidence-based practice and improved patient care in breast oncology.

Key words: Benign, evidence-based, fibroepithelial, phyllodes tumor

INTRODUCTION

Phyllodes tumors (PTs) are rare fibroepithelial skin lesions. They account for 0.3–0.5% of female breast tumors.[1] The incidence is around 2.1/million, with a peak among women aged 45–49 years.[2,3] The tumor is uncommonly detected in adolescents or the elderly. Giant fibroadenomas were first described in 1774.[4] The word "phyllodes tumor" refers to a range of fibroepithelial diseases. The inclusion of epithelial and stromal constituents separates PTs among other forms of sarcomas. Pre-operative pathology diagnosis ensures accurate surgical planning and prevents the need for reoperation for broader excision or tumor recurrence.[5-7] Inadequate treatment of carcinogenic tumors of the phyllodes can result in rapid growth and dissemination of metastatic disease. Benign PTs resemble fibroadenomas and can be managed with local surgery. PTs must be distinguished from different benign breast diseases, especially since fibroadenomas are frequently treated non-operatively. Treatment options include extensive local excision or mastectomy with histologically clean margins.[2,8,9]

EPIDEMIOLOGY

PTs account for 0.3–1% of all breast tumors and 2.5% of all fibroepithelial breast tumors.[2] They predominantly affect

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women between 35 and 55 years of age, with a median age of presentation slightly older than that of fibroadenomas.[10] Although rare, malignant PTs are responsible for a small percentage of breast sarcomas.[11]

ETIOLOGY

The specific cause of PT and its association with fibroadenoma remains unknown.[12]

Most fibroadenomas feature polyclonal elements, indicating they are hyperplasic rather than malignant tumors. A somatic mutation in fibroadenomas can lead to monoclonal proliferation, which is histologically similar to polyclonal elements, but Clonal research indicates a higher risk of local relapse and progression into a PT. It has also been proposed that stromal promotion of cancers of the phyllodes occurs as a result of growth factors released by the breast epithelium. Trauma, the lactation period, and enhanced estrogen activity are sometimes identified as variables that promote tumor development. The nature of these factors is unclear, but endothelin-1, a stimulator of breast fibroblast growth, may be important.[13] Genetic mutations involving MED12, also implicated in fibroadenomas, have been identified in PTs, particularly benign variants.[11]

PATHOPHYSIOLOGY

PTs develop from the periductal stroma and include both epithelial and stromal components. The hallmark is a hypercellular stroma that pushes and distorts the epithelial-lined channels, resulting in the typical "leaf-like" protrusion. The stromal component mostly influences PTs' biologic behavior, which may demonstrate atypia, a high mitotic rate, and infiltrative margins in malignant cases.[14] These lesions differ from fibroadenomas by having significant stromal expansion and hypercellularity. Histologic features, such as stromal cellular atypia, mitotic activity, stromal overgrowth, tumor margin type (confined vs. infiltrative), and tumor necrosis determine whether a lesion is benign, borderline, or malignant.[15] The epithelial component of PTs expresses estrogen and progesterone receptors, whereas the stromal component does not.[16,17]

CLASSIFICATION

The World Health Organization (WHO) categorizes PTs into three kinds based on histological criteria [Table 1].

- Benign: Mild stromal cellularity, minimal atypia, <5 mitoses/10 high power fields (HPFs), pushing borders
- Borderline: Substantial peripheral cellularity and atypia, 5–9 mitoses/10 HPF, with potential infiltrative margins
- Malignant: Marked stromal cellularity and atypia, ≥10 mitoses/10 HPF, stromal overgrowth, infiltrative margins.[18]

These histological findings are critical for directing treatment and predicting outcomes, such as recurrence or metastasis. The WHO's classification is widely used in clinical pathology and surgical oncology.[19]

DIAGNOSIS

Clinical presentation

The tumor typically affects this cancer, typically affects women around the ages of 35 and 55 (approximately 20 years later than fibroadenoma) and is more prevalent in Hispanic American, Caucasian, and Asian populations. Several instances have been described in male, and they are usually associated with gynecomastia. It typically appears as a quickly developing, relatively benign breast lump. In certain cases, a lesion may be present for years before presenting clinically as a dramatic increase in size.[14,20]

Phyllodes lesions typically show as fast expanding, asymptomatic breast masses that are frequently mistaken for fibroadenomas, particularly in the early stages. A mass is generally mobile, and well-circumscribed, but larger tumors may stretch the skin or cause skin ulceration, particularly in malignant forms. Most cases are unilateral, and axillary lymph node involvement is rare, even in malignant types[10,14,21] [Table 2].

Patient demographics

- Age: Typically, women aged 35–55 years
- History: May have prior fibroadenomas or a history of excised breast lumps.[22,23]

Radiological investigations

Mammography and ultrasonography are the most commonly used imaging techniques for breast lumps.[24] Common characteristics include round shapes, well-defined borders, varied interior structure and non-enhancing interior septations in PTs rather than fibroadenomas.

Ultrasonography

The lobulated shape is clearly identified with smoother boundaries, an echogenic rim, and low-level, uniform inner echoes. Fluid-filled clefts in a solid mass, indicating PT, with strong transmission and no microcalcification are observed.[25,26]

Table 1: Histological classification features for phyllodes tumor

Criteria	Benign	Borderline	Malignant
Tumor boundary	Well-defined	May show areas of both well-defined and infiltrative borders	Poorly defined, infiltrative into the surrounding tissue
Stromal cell density	Sparse stromal cells	Moderately increased stromal cells	Densely packed stromal cells
Cell division rate (per 10 HPF)	Fewer than 5 cell divisions	Between 5 and 9 cell divisions	10 or more cell divisions
Cellular Atypia (Pleomorphism)	Mild variation in cell shape and size	Moderate abnormalities in cell appearance	Marked variation with highly abnormal-looking cells

Table 2: Common clinical features

Feature	Description
Palpable mass	Most common symptom: Firm, mobile, well-demarcated
Rapid growth	Fast enlargement over weeks to months
Size at presentation	Often>3–5 cm; can exceed 10 cm (referred to as "giant PTs")
Skin changes	Skin stretching, shiny appearance, or ulceration (rare)
Pain	Usually absent; dull pain in some large tumors
Nipple discharge or retraction	Rare
Axillary lymphadenopathy	Rare even in malignant PTs; mostly reactive, not metastatic

Mammography

i. A well-defined lobulated mass with rounded edges
ii. Compression of the surrounding tissue may result in a visible ring around the lesion
iii. Granular calcification (carcinoma microcalcification is infrequent) can develop.[25,27,28]

Core needle biopsy

Breast biopsy core needle specimens with fibroepithelial lesions and cellular stroma can result in fibroadenoma or PT after excision. The diagnosis is based on stromal cellularity and the stroma-to-epithelium ratio. PTs differ from fibroadenomas because of increased stromal cellularity and mitotic activity.[29]

MANAGEMENT

PTs are primarily managed surgically, as these malignancies have a predisposition for local recurrence and, in the malignant type, a danger of distant metastasis.

The extent of surgery and the need for adjuvant therapy depend on histological grade, tumor size, margin status, and recurrence history (Table 3).

Surgical management

a. Wide local excision (WLE)
- Primary treatment for all grades of PT
- Adequate surgical margins of ≥1 cm are recommended to prevent recurrence
- Even benign PTs should be widely excised, as incomplete excision is associated with recurrence.[8,14]

b. Mastectomy
- Indicated when:
  - The tumor is too large for breast conservation
  - Recurrent tumor after previous excisions
  - Inadequate margins are not possible with WLE
- Not associated with better survival in malignant PT, but helps local control in giant tumors.[30]

c. Axillary surgery
- Not routinely performed
- The fluid involvement is uncommon, even in malignant PT
- Axillary dissection only if nodes are clinically palpable.[31]

Radiotherapy

- May be considered in borderline PTs, especially when:
  - Surgical edges are close or positive
  - The tumor is recurrent
  - Tumor is ≥5 cm
- Shown to reduce local recurrence rates, but no confirmed survival benefit.[32,33]

Chemotherapy

- No established role in the adjuvant setting
- May be used in metastatic or unresectable malignant PTs, based on soft tissue sarcoma protocols

Table 3: Summary table

Treatment modality	Indication	Outcome/comments
Wide local excision	All grades with ≥1 cm margin	First-line treatment reduces recurrence
Mastectomy	Large, recurrent, or margin-negative not achievable	Used for local control
Radiotherapy	Borderline/malignant, recurrent, or close margins	Lowers recurrence but no survival benefit
Chemotherapy	Metastatic malignant PT	Based on sarcoma protocols, limited evidence
Hormonal therapy	Not effective	Not used despite occasional receptor positivity
Follow-up	Regular imaging and clinical exam	Important for the early detection of recurrence

- Agents used include doxorubicin, ifosfamide, and dacarbazine.[34,35]

Hormonal therapy

- PTs do not respond to hormonal therapy, despite occasional hormone receptor positivity in the epithelial component.
- Hormonal treatment is not recommended.[36]

Follow-up and recurrence management

- Most recurrences occur within 2–3 years post-surgery
- Conduct regular clinical exams and imaging every half month for the first 3 years, then yearly
- Recurrence treated with repeat wide excision or mastectomy.[36,37]

CONCLUSION

Phyllodes lesions in the breast are atypical fibroepithelial malignant tumors that pose a unique therapeutic challenge due to their diverse histology and unexpected biological function. These tumors, which can be benign or malignant, are composed of both epithelial and stromal parts. Despite their resemblance to fibroadenomas on imaging and, in some circumstances, core biopsy, PTs are characterized with their ability to develop rapidly, recur locally, and, in malignant situations, disseminate metastatically – primarily through hematogenous routes.

The cornerstone of treatment remains surgical excision with wide margins, regardless of tumor grade. Achieving clear margins (preferably ≥1 cm) is critical in reduce the risk of local relapse, which remains the common complication. While benign tumors often have a favorable prognosis, borderline and malignant lesions carry a risk of recurrence and metastasis, necessitating a more aggressive surgical approach and, in some cases, consideration of adjuvant radiotherapy. A crucial part of chemotherapy remains limited and is generally reserved for unresectable or metastatic malignant cases, where treatment mirrors that of soft tissue sarcomas.

A key challenge in managing PTs lies in the limitations of pre-operative diagnosis. Imaging and needle biopsy often fail to distinguish them reliably from fibroadenomas, especially in early or benign cases. This underscores the importance of clinical suspicion, particularly when encountering rapidly growing breast masses in women beyond adolescence.

The hormonal therapies are ineffective, despite occasional hormone receptor expression, due to the stromal origin of the neoplastic component.

Long-term follow-up is essential, especially during the first 2–3 years post-treatment, when most recurrences occur. Malignant PTs, while rare, can metastasize to the lungs, bones, or liver, and require vigilant systemic surveillance in high-risk cases.

From a research perspective, recent discoveries in molecular pathology, such as MED12 mutations, offer potential insights into tumorigenesis and may help develop future targeted therapies or improve diagnostic precision. However, clinical application of these findings remains in early stages.

In conclusion, PTs demand a tailored, multidisciplinary approach that balances effective local control with the prevention of overtreatment. As our understanding of their molecular and histological features evolves, so too will our strategies for optimal patient outcomes.

REFERENCES

1. Rowell MD, Perry RR, Hsiu JG, Barranco SC. Phyllodes tumors. Am J Surg 1993;165:376-9.
2. Salvadori B, Cusumano F, Del Bo R, Delledonne V, Grassi M, Rovini D, *et al*. Surgical treatment of phyllodes tumors of the breast. Cancer 1989;63:2532-6.
3. Bernstein L, Deapen D, Ross RK. The descriptive epidemiology of malignant cystosarcoma phyllodes tumors of the breast. Cancer 1993;71:3020-4.
4. Fiks A. Cystosarcoma phyllodes of the mammary gland-Müller's tumor. For the 180th birthday of Johannes Müller. Virchows Arch A Pathol Anat Histol 1981;392:1-6.
5. Ridgway PF, Jacklin RK, Ziprin P, Harbin L, Peck DH, Darzi AW, *et al*. Perioperative diagnosis of cystosarcoma

phyllodes of the breast may be enhanced by MIB-1 index. J Surg Res 2004;122:83-8.
6. El-Naggar AK, Mackay B, Sneige N, Batsakis JG. Stromal neoplasms of the breast: A comparative flow cytometric study. J Surg Oncol 1990;44:151-6.
7. Jacklin RK, Ridgway PF, Ziprin P, Healy V, Hadjiminas D, Darzi A. Optimising preoperative diagnosis in phyllodes tumour of the breast. J Clin Pathol 2006;59:454-9.
8. Chaney AW, Pollack A, McNeese MD, Zagars GK, Pisters PW, Pollock RE, *et al*. Primary treatment of cystosarcoma phyllodes of the breast. Cancer 2000;89:1502-11.
9. Kapiris I, Nasiri N, A'Hern R, Healy V, Gui GP. Outcome and predictive factors of local recurrence and distant metastases following primary surgical treatment of high-grade malignant phyllodes tumours of the breast. Eur J Surg Oncol 2001;27:723-30.
10. Tan PH, Jayabaskar T, Chuah KL, Lee HY, Tan Y, Hilmy M, *et al*. Phyllodes tumors of the breast: The role of pathologic parameters. Am J Clin Pathol 2005;123:529-40.
11. Piscuoglio S, Murray MP, Fusco N, Marchiò C, Loo FL, Martelotto LG, *et al*. MED12 somatic mutations in fibroadenomas and phyllodes tumors of the breast. Hum Pathol 2015;46:1211-8.
12. Noguchi S, Motomura K, Inaji H, Imaoka S, Koyama H. Clonal analysis of fibroadenoma and phyllodes tumor of the breast. Cancer Res 1993;53:4071-4.
13. Azzopardi JG, Ahmed A, Millis RR. Problems in breast pathology. Major Probl Pathol 1979;11:1-466.
14. Reinfuss M, Mituś J, Duda K, Stelmach A, Ryś 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.
15. Telli ML, Horst KC, Guardino AE, Dirbas FM, Carlson RW. Phyllodes tumors of the breast: Natural history, diagnosis, and treatment. J Natl Compr Canc Netw 2007;5:324-30.
16. Dacic S, Kounelis S, Kouri E, Jones MW. Immunohistochemical profile of cystosarcoma phyllodes of the breast: A study of 23 cases. Breast J 2002;8:376-81.
17. Tse GM, Lui PC, Scolyer RA, Putti TC, Kung FY, Law BK, *et al*. Tumour angiogenesis and p53 protein expression in mammary phyllodes tumors. Mod Pathol 2003;16:1007-13.
18. WHO Classification of Tumours Editorial Board. WHO Classification of Tumours of the Breast. 5th ed. Lyon: IARC; 2019.
19. Azzopardi JG, Ahmed A, Millis RR. Problems in breast pathology. Major Probl Pathol 1979;11:1-466.
20. Chua CL, Thomas A, Ng BK. Cystosarcoma phyllodes: A review of surgical options. Surgery 1989;105:141-7.
21. Foxcroft LM, Evans EB, Porter AJ. Diagnosis and management of phyllodes tumours of the breast: Experience of 33 cases at a specialist centre. Aust N Z J Surg 2007;77:230-3.
22. Parker SJ, Harries SA. Phyllodes tumours. Postgrad Med J 2001;77:428-35.
23. Chao TC, Lo YF, Chen SC, Chen MF. Sonographic features of phyllodes tumors of the breast. Ultrasound Obstet Gynecol 2002;20:64-71.
24. Wurdinger S, Herzog AB, Fischer DR, Marx C, Raabe G, Schneider A, *et al*. Differentiation of phyllodes breast tumors from fibroadenomas on MRI. AJR Am J Roentgenol 2005;185:1317-21.
25. Feder JM, De Paredes ES, Hogge JP, Wilken JJ. Unusual breast lesions: Radiologic-pathologic correlation. Radiographics 1999;19:S11-26.
26. Cole-Beuglet C, Soriano R, Kurtz AB, Meyer JE, Kopans DB, Goldberg BB. Ultrasound, X-ray mammography, and histopathology of cystosarcoma phylloides. Radiology 1983;146:481-6.
27. Jorge Blanco A, Vargas Serrano B, Rodríguez Romero R, Martínez Cendejas E. Phyllodes tumors of the breast. Eur Radiol 1999;9:356-60.
28. Cosmacini P, Veronesi P, Zurrida S, Bartoli C, Ferranti C, De Yoldi GC. Mammography in the diagnosis of phyllodes tumors of the breast. Analysis of 99 cases. Radiol Med 1991;82:52-5.
29. Komenaka IK, El-Tamer M, Pile-Spellman E, Hibshoosh H. Core needle biopsy as a diagnostic tool to differentiate phyllodes tumor from fibroadenoma. Arch Surg 2003;138:987-90.
30. Belkacémi Y, Bousquet G, Marsiglia H, Ray-Coquard I, Magné N, Malard Y, *et al*. Phyllodes tumor of the breast. Int J Radiat Oncol Biol Phys 2008;70:492-500.
31. 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.
32. Barth RJ Jr., Wells WA, Mitchell SE, Cole BF. A prospective, multi-institutional study of adjuvant radiotherapy after resection of malignant phyllodes tumors. Ann Surg Oncol 2009;16:2288-94.
33. Gnerlich JL, Williams RT, Yao K, Jaskowiak N, Kulkarni SA. Utilization of radiotherapy for malignant phyllodes tumors: Analysis of the National cancer data base, 1998-2009. Ann Surg Oncol 2014;21:1222-30.
34. Spitaleri G, Toesca A, Botteri E, Bottiglieri L, Rotmensz N, Boselli S, *et al*. Breast phyllodes tumor: A review of literature and a single center retrospective series analysis. Clin Breast Cancer 2013;13:62-9.
35. Hawkins RE, Schofield JB, Fisher C, Wiltshaw E, McKinna JA, Gazet JC, *et al*. Metastatic malignant cystosarcoma phyllodes of the breast. Br J Cancer 1992;65:227-30.
36. Tan PH, Jayabaskar T, Chuah KL, Lee HY, Tan Y, Hilmy M, *et al*. Phyllodes tumors of the breast: The role of pathologic parameters. Histopathology 2005;47:34-40.
37. Guillot E, Couturaud B, Reyal F, Curnier A, Ravinet J, Laé M, *et al*. Management of phyllodes breast tumors. Breast Cancer Res Treat 2011;129:771-9.

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