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Transformation of Malignant Phyllodes Tumors into Benign Tumors in Tumor Recurrence: A Case Report

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Abstract

Objective: Phyllodes tumors (PTs) are rare, distinctive fibroepithelial neoplasms. They are associated with a low incidence and comprise 0.3% - 0.9% of all breast tumors. Recurrence occurs in about 20% of cases, and malignant PTs exhibit a higher rate of early recurrence than benign ones. The transformation from malignant to benign PTs is extremely rare. Here, we presented the case of a 29-year-old woman diagnosed with a malignant PT that transformed into a benign Within six months after excisional surgery. **Materials and Methods:** This is a case report. **Results:** A 29-year-old woman presented to our hospital with left breast enlargement, which was not accompanied by pain or discharge. An ultrasound revealed a heterogeneous, solid mass. She underwent surgical excision of the mass, which was later diagnosed as a malignant PT pathology. After the surgery, the patient was monitored through regular follow-up visits, during which all examinations were normal. However, six months later, a new mass was felt in the same area. She underwent another surgical excision, and this mass was diagnosed as a benign PT. **Conclusion:** Malignant PTs should be taken into account for patients who present with rapidly growing breast masses. Timely diagnosis and treatment are vital because they significantly affect the prognosis of these cases. A thorough evaluation, including ultrasound and biopsy, is necessary to prevent misdiagnosis. The definitive diagnosis of PTs can only be established through biopsy. Effective treatment, which involves surgical excision with clear margins, is crucial for preventing recurrence and

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potentially life-threatening consequences.

Keywords

Phyllodes Tumor of the Breast, Breast Neoplasms, Neoplasm Recurrence, Local

1. Introduction

Phyllodes tumors (PTs) are uncommon and unique fibroepithelial tumors with a low incidence rate, which account for 0.3% - 0.9% of all breast tumors. They are most frequently observed in women aged 40 to 50. According to their histological features, such as stromal overgrowth, cellularity, atypia, mitotic activity per high-power field, and tumor margins, PTs are categorized as benign, borderline, or malignant. Benign PTs are more prevalent than the other grades. Traditionally, the recommended treatment for PTs has involved surgical excision with a clear margin of at least 1 cm.

Tumor sizes have been reported to range from 1 to 40 cm, with about 20% of patients presenting with masses larger than 10 cm. The five-year survival rates are nearly 100% for benign PTs, 98% for borderline PTs, and about 88% for malignant PTs. A PT is classified as "giant" if it exceeds 10 cm in size. Treatment options may differ based on factors, such as malignant potential, recurrence, resection margin status, and tumor size, ranging from wide local excision with at least 1 cm of surrounding breast tissue to radiotherapy. [1]

The behavior of PT is unpredictable. Also, there is no definite correlation between their clinical behavior and histopathological features, and there is genetic heterogeneity among tumors. [2]

Recurrence occurs in less than 20% of cases, and earlier recurrence is more common in malignant PTs compared to benign PTs. Phyllodes tumors typically metastasize through the bloodstream to organs such as the liver, heart, skeleton, and lungs. Local recurrence generally occurs within the first few years following surgery. [3]

The transformation from a malignant PT to a benign one is an extremely rare occurrence in breast cancer. [4] We reported the case of a 29-year-old woman diagnosed with a PT that transformed into a benign one approximately six months after excisional surgery.

2. Case Presentation

A 29-year-old woman visited Besat Hospital in Hamedan, Iran, in February 2022, with complaints of left breast enlargement. She reported no pain or discharge. Upon examination, a firm lump was detected. The patient had no family history of breast cancer. An ultrasound was conducted, which showed a heterogeneous, solid mass. The lesions were indistinguishable from fibroadenomas on both mammograms and

ultrasound; thus, surgical excision was advised, and the mass was sent for pathological evaluation.

The tumor measured 16 × 15 × 11 cm at its largest dimension. The pathology report indicated a well-circumscribed breast neoplasm with spindle cell proliferation, with all margins involved except for the inferior margin. It also noted increased cellularity, stromal overgrowth, and mild to moderate stromal atypia. The final diagnosis was a malignant PT. Fortunately, no lymph node involvement was found; thus, lymph node dissection was not performed (Figure 1).

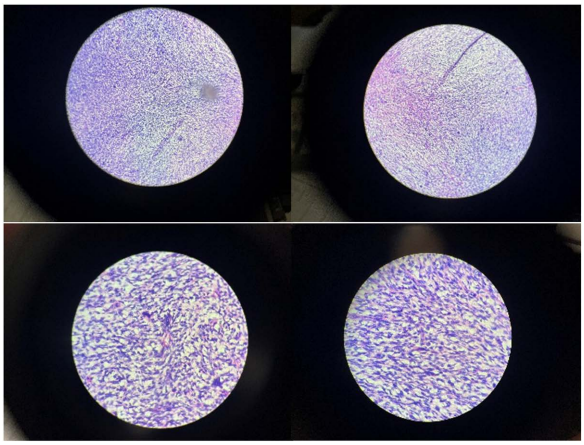

Figure 1. Malignant phyllodes pathology slide.

After the surgery, the patient was closely monitored and attended follow-up appointments with her surgeon every three months at the breast cancer clinic in Besat Hospital. All examinations during this period were normal. However, a new mass was detected at the same location six months later during a routine check-up. She was scheduled for an excisional biopsy. After the second surgical excision, the specimen was sent for histopathological analysis. The pathology report identified fibroepithelial breast neoplasm characterized by stromal cell proliferation with no atypia. Multi-focal infiltration into normal mammary lobules was noted. The tumor measured 3 × 2.8 × 2.5 cm, and there were no involved margins (Figure 2). The final diagnosis was a benign PT. After the second surgery, the patient continued her regular follow-up visits with her surgeon, and to date, there has been no evidence of recurrence or metastasis.

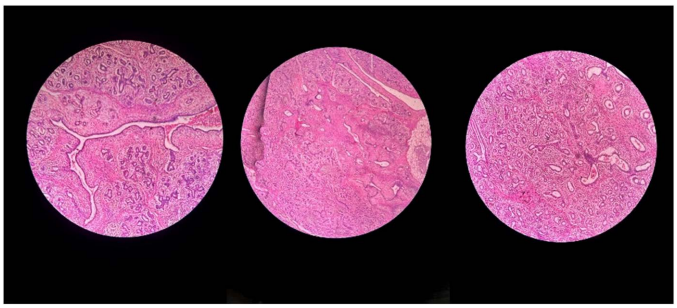

Figure 2. Benign phyllodes pathology slide.

3. Discussion

Breast cancer is the second leading cause of cancer-related deaths among women, with one in nine women being diagnosed during their lives. [5] Breast PTs are rare and account for less than 1% of all breast tumors. They typically appear as rapidly enlarging breast masses and have histological characteristics similar to those of fibroadenomas. [6] These tumors are most frequently found in women between the ages of 40 and 50. [7] Clinically, PTs usually present as painless, growing masses that contain both epithelial and stromal components. While local recurrence is relatively common, metastasis is rare and occurs almost exclusively in malignant PTs, which are often misdiagnosed as fibroadenomas. [8] [9]

The World Health Organization (WHO) categorizes PTs into benign, borderline, and malignant types based on various histological criteria, including stromal hypercellularity, tumor margins, cytological atypia, mitotic activity, and stromal overgrowth (**Table 1**). [9] Recurrence rates vary significantly among these categories, with reported rates of 11.2% for benign PTs, 15.9% for borderline PTs, and 24.5% for malignant PTs. Distant metastases are nearly absent in benign PTs, occur in under 2% of borderline PTs, and are seen in around 16% of malignant PTs. [10]

Table 1. The World Health Organization classification of phyllodes tumors.

Criteria	Benign	Borderline	Malignant
Tumor border	Well-defined	Well-defined; maybe focally infiltrative	Infiltrative
Stromal cellularity	Cellular, usually mild	Cellular, usually moderate	Cellular, usually marked and diffuse
Stromal cell atypia	None to mild	Mild or moderate	Marked
Mitotic activity	Less than 5 per HPF	5 - 9 per HPF	More than10 per HPF
Stromal overgrowth	Absent	Absent or very focal	Often present
Malignant heterologous elements	Absent	Absent	May be present

Unfortunately, patients with metastases typically do not respond well to chemotherapy and often die within three years of diagnosis. Important histological and pathological factors associated with metastasis include tumor size exceeding 7 cm, significant stromal overgrowth, infiltrative borders, high stromal cellularity, more than 5 five mitoses per ten high-power fields (HPF), and necrosis. [11] In our patient's pathology report, several high-risk features were identified: the tumor measured over 7 cm, exhibited stromal overgrowth, had 7 mitoses per 10 HPF, and showed evidence of hemorrhagic necrosis (**Figure 1**).

The relationship between genetic changes and the histological and pathological features of PTs is not entirely clear. It is suggested that epithelial-stromal interactions, particularly the expression of β-catenin and insulin-like growth factors

(IGF-I and IGF-II) in the stroma, may contribute to the development of PTs. Additionally, the Ki67 marker could be valuable for tumor grading and prognostic assessment. [9]

While fibroadenomas are more prevalent in Black women, it remains uncertain whether this trend applies to PTs due to their rarity and limited race-related data. [12] Differential diagnosis of PTs depends on histological and pathological patterns. Benign PTs can be misdiagnosed as fibroadenomas, whereas malignant PTs might be confused with primary breast sarcomas. [9] Clinical examination, along with imaging techniques such as mammography and ultrasound, is crucial for diagnosis, although they often fall short in differentiating PTs from fibroadenomas. Core needle biopsy can also provide useful information, but because of overlapping features and tumor heterogeneity, it can sometimes yield misleading results. Given these diagnostic challenges, we opted to perform an excisional biopsy on our patient, who presented with a growing mass but had no conclusive findings on ultrasound (**Figure 1**) [13].

Surgical excision remains the primary treatment for PTs, even when the diagnosis is only suspected. If the final pathology confirms the presence of a PT, re-excision with wider margins may be required. Breast conservation is the preferred strategy when oncological and aesthetic outcomes can be achieved. [13] [14] However, mastectomy is frequently recommended, especially for larger tumors, as nearly 50% of cases involving tumors larger than 5 cm result in mastectomy using advanced oncoplastic techniques. Since PTs spread through the bloodstream, axillary nodal sampling is not necessary unless there is evidence of lymph node involvement, even in malignant cases [13] [15].

The use of chemotherapy or radiotherapy in the treatment of phyllodes tumors is debated, leading the medical team to opt for surgery only for the patient. [16]

After discussing the options, the surgeon and the patient agreed that the patient would not undergo a mastectomy but would instead proceed with an excisional biopsy.

In our patient's case, a surgical excision with a 1 cm margin was performed, and she was closely monitored afterward. Six months after the initial surgery, during a routine follow-up, another mass was detected. After a second surgery, the patient was diagnosed with a benign phyllodes tumor. She continues to be monitored regularly, with no further abnormalities found.

To accurately evaluate breast masses, it is crucial to monitor their growth rates. A growth rate exceeding 20% within six months may suggest a PT rather than a fibroadenoma, which would require surgical excision or biopsy. Although rapidly enlarging large masses are indicative, a biopsy is still necessary to confirm the diagnosis. [17]

Diagnosis of PTs presents a unique challenge due to their rarity, overlapping characteristics with fibroadenomas, and diverse clinical behavior. The frequent misdiagnosis of PTs as fibroadenomas underscores the complexities involved in diagnosing these tumors. Both conditions exhibit similar histological features,

including a biphasic pattern of epithelial and stromal components, which complicates initial clinical assessments. While core needle biopsies are commonly used, they may not effectively distinguish between fibroadenomas and PTs due to the heterogeneity of the tumors. Excisional biopsies, as conducted in this case, are considered the gold standard for diagnosis, especially for large or rapidly growing tumors, as they provide a more thorough histological analysis.

Recurrence rates for PTs vary significantly among different studies. According to the WHO, recurrence rates are reported to be between 10 - 17% for benign PTs, 14 - 25% for borderline PTs, and 23 - 30% for malignant PTs. [18] Local excision is the primary treatment option aimed at preserving normal breast tissue; however, the presence of residual tumor cells can result in recurrence. Recurrent tumors are usually histologically similar to the original tumor. Clinicians must remain vigilant, as all types of PTs have the potential to recur, occasionally showing atypical changes. [4]

In cases of malignant PTs, negative margins must be achieved to reduce the high rate of recurrence and mortality (approximately 22%). In contrast, benign PTs can often be managed with close observation, even if positive margins are present. [17] Some studies report that adolescents have a higher risk of recurrence, warranting close monitoring even when margins are negative. [19] Additionally, ethnicity may play a role in the recurrence of PTs, with some studies suggesting that Asian women are at higher risk of recurrence compared to non-Asians. [20] For malignant PTs, achieving negative margins is essential to decrease the high rates of recurrence and mortality, which is approximately 22%. In contrast, benign PTs can often be managed with careful observation, even in cases where positive margins are present. Some studies indicate that adolescents may have a higher risk of recurrence, necessitating close monitoring even when margins are negative. Additionally, ethnicity may influence the recurrence of PTs, with some research suggesting that Asian women are at a greater risk of recurrence compared to non-Asians.

The recurrence in our case highlights the importance of obtaining wider margins in certain patients, particularly those who have large tumors, to reduce the risk of regrowth.

Overall, PTs have a favorable prognosis. The five-year survival rate for patients with benign and borderline tumors is approximately 91%, whereas the survival rate for those with malignant PTs is about 82%. [21]

4. Conclusion

PTs should be considered when evaluating rapidly growing breast lumps. Early diagnosis and treatment are vital because they can significantly affect the prognosis. A thorough evaluation, including ultrasound and biopsy, is necessary to avoid misdiagnosis, and biopsy is the only definitive method for diagnosing PTs. Patients diagnosed with PTs require close follow-up, as recurrence is a common concern. Given the ongoing debate regarding the role of chemotherapy and radiotherapy,

the medical team must carefully determine the most suitable treatment approach. There is a growing trend toward breast-conserving surgery when oncologically appropriate, allowing for effective cancer treatment while also maintaining aesthetic results. However, surgical excision with at least a 1 cm margin is essential to reduce the risk of recurrence and mortality. Early detection, timely treatment, and routine follow-up are effective strategies for improving survival rates in patients with PTs.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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