Case Report

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Malignant transformation of recurrent benign phyllodes tumor: a case report and comprehensive review of literature

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Introduction: Phyllodes tumors (PTs) of the breast are rare fibroepithelial neoplasms, accounting for less than 1% of all breast tumors. The WHO classifies PTs into benign, borderline, or malignant categories based on histological features. While benign PTs generally have a favorable prognosis, they carry a risk of transformation into malignant variants, particularly in cases of recurrence.
Case presentation: A 33-year-old female presented with a recurrent benign PT, previously treated with lumpectomy on two occasions. Recent imaging suggested possible malignant transformation, and histopathological examination confirmed a malignant PT.
Discussion: This case highlights the crucial role of imaging in the early detection of malignant transformation in PTs. Surgical management strategies are discussed, with an emphasis on the potential for recurrent benign tumors to progress to malignancy.
Conclusion: Regular imaging and close follow-up are essential for early detection of malignant transformation in recurrent PTs, guiding timely and appropriate surgical intervention.

Keywords: case report, malignant transformation, mammography, recurrent phyllode tumor, stromal overgrowth

Introduction

Phyllodes tumors (PTs) comprise less than 1.0% of all primary breast tumors[1]. Approximately 75% of PTs are benign, while 16% are borderline low-grade and 9% are malignant high-grade [2]. In Los Angeles county, the average yearly incidence rate of malignant PTs over a 17-year period was 2.1 per million women[3]. Although the etiology remains unclear, some tumors may rarely develop within fibroadenomas[4]. PTs generally occur in an older population compared to fibroadenomas, with a median age of 45–49 years. While predominantly affecting women, a few cases have been reported in men[5].

Benign PTs have a favorable prognosis and are usually well-managed with surgery, with a local recurrence rate of about 10.0–20.0%[6,7]. However, malignant and occasionally borderline PTs can exhibit more aggressive behavior, with local recurrence rates for malignant PTs ranging from 15.0 to 40.0%[8]. Distant metastasis is rare, occurring almost exclusively in malignant PTs at a rate of 9.0–27.0%, and primarily spreading through the hematogenous route[8].

HIGHLIGHTS

- Phyllodes tumors (PTs) are rare fibroepithelial neoplasms that account for less than 1% of all breast tumors.
- Benign PTs carry a risk of malignant transformation, particularly in recurrent cases, as demonstrated in this case of a 33-year-old female with a recurrent benign PT that transformed into a malignant variant.
- While few patients of PTs may have palpable axillary lymphadenopathy, most cases are reactive, and lymph node metastasis in PTs is rare.
- Radiology is essential for identifying the suspicious features of malignant PTs and assessing the extent of the disease but histopathology remains the gold standard for differentiating benign from malignant PTs.
- Regular imaging and close follow-up are crucial for timely intervention, reducing the risk of progression in recurrent PTs.

We present the case of a 33-year-old female with a recurrent left breast lump, who had previously undergone lumpectomy twice for recurrent benign phyllode tumor (PT). Recent imaging raised suspicion of malignancy, and subsequent histopathological examination confirmed a diagnosis of malignant PT. This case underscores the critical role of imaging in the early detection of malignant transformation in PTs, highlights surgical considerations, and emphasizes the potential for recurrent benign PTs to evolve into malignant ones. The case has been reported in line with the Surgical CAse Report (SCARE) 2023 criteria[9].

Case presentation

A 33-year-old female presented with a progressively growing left breast lump for several months, which recently increased rapidly

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in size and became painful over the span of a few weeks. She had a history of recurrent benign PT of the left breast (Figs 1A and B), for which she had undergone lumpectomy twice, with an interval of 2 years between surgeries, the last one being 2 years ago. On examination, the left breast appeared bosselated with slit-like retraction of the nipple. Palpation revealed an irregular, firm, tender, mobile mass involving nearly all quadrants of the left breast. A few lymph nodes were palpable in the left axilla. The patient's vital signs and basic laboratory parameters were essentially normal.

Mammography (Figs 2A and B) showed a large, irregular, high-density mass involving all quadrants of the left breast, measuring 14×11×10 cm, with partially indistinct margins. Diffuse skin thickening was observed in the periareolar region and lower inner quadrant of the breast, but no internal calcifications were noted. Ultrasound (Fig. 2C) revealed a large, irregular, heteroechoic mass with microlobulated margins and significant internal vascularity in the left breast. Contrast-enhanced computed tomography (CT) (Figs 3A and B) revealed an asymmetric, large left breast with a heterogeneously enhancing conglomerate of multiple soft tissue density masses. The mass had an indistinct plane with the skin, accompanied by skin thickening. Few enhancing lymph nodes were observed in both axillae, with maintained fatty hilum. These features raised suspicion for malignancy. A core-cut needle biopsy from the breast mass was performed, which revealed a malignant PT. Since the ultrasound and CT morphology of the lymph nodes appeared benign and PTs typically do not metastasize to lymph nodes, FNAC (fine needle aspiration cytology) was not performed.

Given the history of recurrent disease despite previous surgeries, the large size of the tumor, malignant histological findings, and the patient's concerns regarding recurrence, a left mastectomy was scheduled for 2 weeks later. Left mastectomy was performed and intraoperatively, multiple visibly enlarged lymph nodes were observed in the left axilla, with both their number and size significantly greater than what had been reported in the imaging 2 weeks earlier. As a result, the surgical team decided to proceed with axillary dissection, even though axillary dissection is not routinely indicated unless the nodes are confirmed to be metastatic by FNAC or biopsy.

Histopathological examination (Figs 4A and B) from multiple sections showed marked cellularity of stromal cells with stromal overgrowth. These cells were spindle-shaped and arranged in diffuse sheets, having scant cytoplasm, ovoid nuclei, vesicular chromatin, and prominent nucleoli. These cells exhibited marked nuclear atypia. Mitotic figures were > 10/10 HPF. Large areas of necrosis were observed. A few scattered glands were lined by two layers of epithelial cells. All lymph nodes were free of tumor involvement. Based on these findings, a final diagnosis of malignant PT was made. The patient subsequently received adjuvant radiotherapy for 5 weeks. Three months postsurgery and radiotherapy, the patient is doing well.

Discussion

PTs can develop slowly, rapidly, or exhibit a biphasic growth pattern. They may grow into a noticeable mass, with sizes ranging from 1 to 45 cm, potentially occupying the entire breast, altering

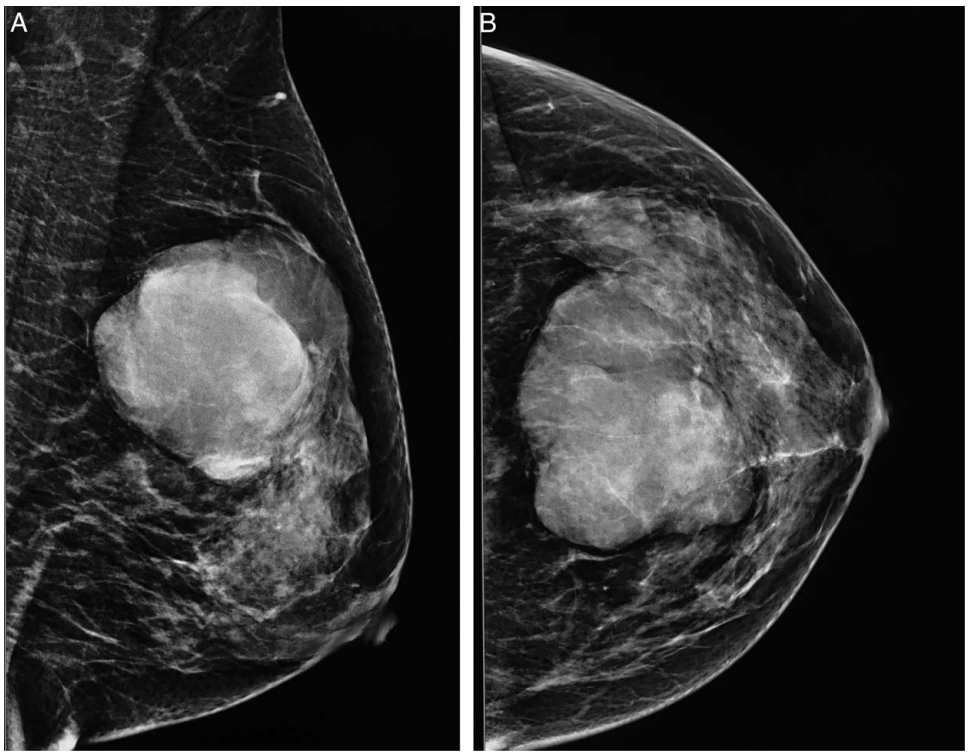

Figure 1. (A and B) Mammography (performed 2 years ago) showing an irregular, high-density mass in the upper central aspect of the left breast, with partially obscured/indistinct margins. No internal calcifications were noted.

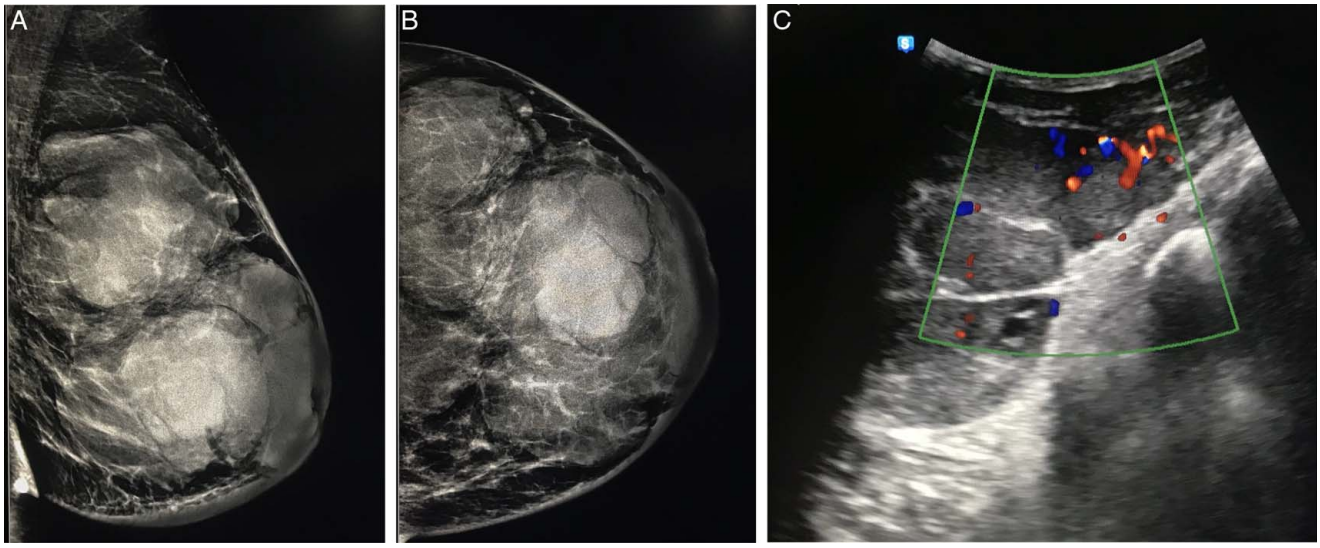

Figure 2. (A and B) Mammography revealed a large, irregular, high-density mass involving all quadrants of the left breast, with partially indistinct margins. Diffuse skin thickening was observed in the periareolar region and lower inner quadrant of the breast, but no internal calcifications were noted. (C) Ultrasound imaging revealed a large, irregular, heteroechoic mass with microlobulated margins and significant internal vascularity in the left breast.

its shape, or causing pressure necrosis of the overlying skin[8]. While ~20% of patients may present with palpable axillary lymphadenopathy, most cases are reactive, and lymph node metastasis in PTs is rare[8].

Imaging findings on mammography typically reveal a round, lobulated, high-density mass with partially indistinct or circumscribed margins. Calcifications within the mass are uncommon, but when present, they can be large[10]. On ultrasound, PTs usually appear as hypoechoic masses with partially indistinct or circumscribed margins and frequent posterior enhancement. Malignant PTs often exhibit more complex features, such as more irregular margins, heterogeneous echotexture, internal cystic components, and thick septations[10]. Malignant tumors also tend to show increased vascularity on Doppler ultrasound[2] and heterogeneous contrast enhancement on CT[11]. In our case, the mammography revealed a large, irregular, high-density breast mass with partially indistinct margins; ultrasound showed an irregular, heteroechoic mass with microlobulated margins and significant internal vascularity, and the CT scan demonstrated heterogeneous contrast enhancement, most findings favoring malignancy.

Benign PTs typically display low signal intensity on T1-weighted images and high signal intensity on T2-weighted images, with homogeneous contrast enhancement and absence of internal complexity. In contrast, malignant PTs show heterogeneous signal intensity on both T1 and T2-weighted images and may contain hyperintense areas on T1 due to hemorrhage. They also exhibit septal enhancement and suspicious features, such as thick septations, internal solid components, cystic spaces, and rapid enhancement on dynamic postcontrast imaging. High signal on diffusion-weighted imaging and low apparent diffusion coefficient values suggest malignancy[12–14]. These imaging differences help guide the diagnosis of PTs, although definitive diagnosis often requires histopathological analysis.

Malignant PTs are pathologically characterized by significant stromal cellularity, more than 10 mitoses per 10 high-power fields, invasive margins, and extensive stromal overgrowth[15].

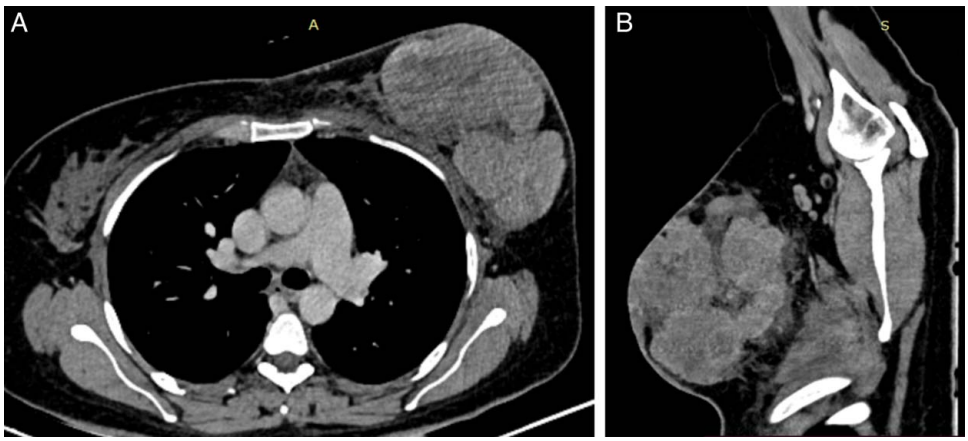

Figure 3. (A and B) Contrast-enhanced computed tomography (CT) revealed an asymmetric, large left breast with a heterogeneously enhancing conglomerate of multiple soft tissue density masses. The mass had an indistinct fat plane with the skin and was accompanied by skin thickening.

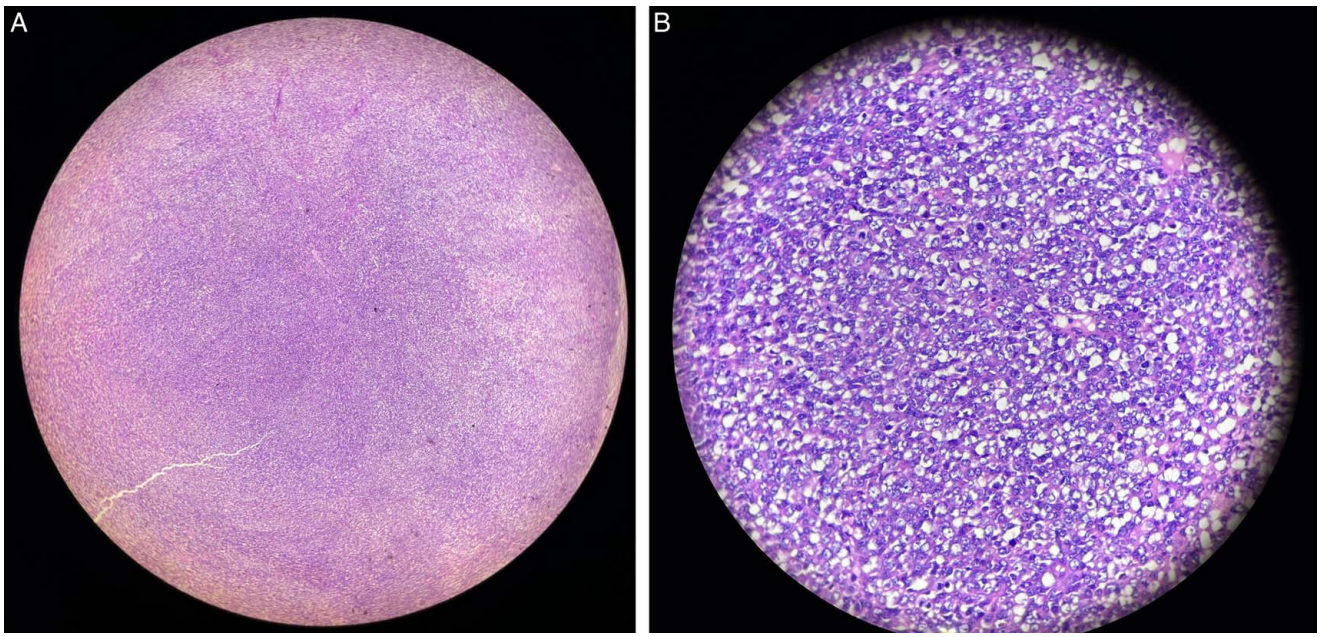

Figure 4. (A) Histopathological examination (Hematoxylin and Eosin (H&E) stain, 50× magnification) showing stromal overgrowth. (B) Histopathological examination (H&E stain, 400× magnification) showing vesicular chromatin, prominent nucleoli, and several mitotic figures.

Core needle biopsy is typically accurate in diagnosing these tumors, although distinguishing PTs from cellular fibroadenomas can be subtle[15–17]. Our case exhibited the findings consistent with malignant PTs.

Complete wide local excision with margins greater than 1 cm is often curative and lowers the risk of local recurrence[18,19]. Mastectomy is indicated in cases of larger tumors, recurrent disease, inability to achieve adequate surgical margins, malignant histology, and patient preferences due to concerns about recurrence[20,21]. Axillary lymph node dissection is not routinely performed unless clinically suspicious or proven metastatic by FNAC or biopsy, as lymph node metastasis is rare in PTs[21]. Adjuvant radiotherapy is typically considered for high-risk patients with PTs, particularly when certain features increase the likelihood of local recurrence, such as positive or close surgical margins, large tumor size, or recurrent tumors[20]. The role of adjuvant chemotherapy in PTs remains controversial and may be considered in select high-risk cases, particularly for malignant PTs with distant metastasis[20,21].

The overall prognosis for PTs is favorable, with an 87% 10-year survival rate. Recurrence risk is influenced by tumor size and surgical method. For instance, the 5-year recurrence after lumpectomy ranges from 9 to 41% for tumors <2 cm compared to 5–10 cm. After mastectomy, the 5-year recurrence ranges from 5 to 12% for tumors <2 cm compared to 5–10 cm[21,22].

Benign PTs can recur and, in some cases, progress to a more aggressive form, including malignant PTs[23]. Malignant transformation, though uncommon, has been documented in recurrent PTs, which may present more aggressively after recurrence[23,24].

The limitations of this case report include the lack of imaging immediately prior to the surgery. An ultrasound could have been performed a few days before the surgery to assess any progression. Additionally, lymph node assessment and subsequent FNAC/biopsy could have been conducted before surgery. This may have resulted in a less invasive procedure, such as a mastectomy instead of a modified radical mastectomy. Another limitation is the short follow-up duration after the recent surgery; longer follow-ups would be necessary to evaluate long-term outcomes.

Conclusion

Radiology is essential for identifying the suspicious features of malignant PTs and assessing the extent of the disease but histopathology remains the gold standard for differentiating benign from malignant PTs, as imaging features often overlap. Benign PTs, though rarely can transform into malignant form, the clinicians should have high index of suspicion, especially in cases of recurrent tumor.

Patent perspective

After undergoing two surgeries, I was optimistic that the lump would not recur. It is really frustrating to have a recurrent lump in the same breast, and now to be diagnosed with a malignant disease. The uncertainty of the disease's progression and the fear of future recurrences are emotionally exhausting. However, I trust that the doctors have made the best decisions for my health, and I hope it does not recur.

Ethical approval

Since this is a case report, our Institutional Review Board Institute of Medicine (IOM) has waived the requirement for ethical approval.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

A.K.: conceptualization, manuscript writing, and literature review; A.B.: literature review, editing S.K.C.: manuscript writing and literature review; U.S. and S.R.: literature review. All authors have read and approved the manuscript.

Conflicts of interest disclosure

The authors report no conflicts of interest.

Research registration unique identifying number (UIN)

Since it is a case report and not a research study, no clinical trials have been performed.

Guarantor

Abhikanta Khatiwada and Aashish Bastakoti.

Data availability statement

It will be open access and publicly available as per the journal's guideline.

Provenance and peer review

Not commissioned, externally peer-reviewed.

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