

Case Report

Three Benign Phyllodes Tumors in a Patient Showing a Serial Multicentric Occurrence Pattern: A Case Report

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Abstract

Phyllodes tumor is a rare lesion of fibroepithelial origin most commonly reported in middle aged women. Historically these tumors have high rates of local recurrence after surgical resection and accepted treatment of these lesions is local excision with wide margins. We present a case of a young woman who has had three serial benign phyllodes tumors in different quadrants of the right breast with no true local recurrences to date. Her age and multicentricity, without local recurrence, are atypical characteristics of phyllodes tumors; to our knowledge, this is the first documented case of a phyllodes tumor occurring, in three separate incidents, in a multicentric pattern. Though phyllodes tumors share multiple characteristics with fibroadenoma lesions, discrimination between the two is pertinent in terms of treatment and prognosis. We recommend that in a young woman whom develops multiple serial lesions at different sites within the same breast, that lesions other than benign fibroadenomas be considered within the differential diagnosis.

Keywords: Phyllodes Tumor; Multicentric; Benign; Fibroadenoma

Introduction

Phyllodes tumor is a rare neoplasm of fibroepithelial origin. Though typically benign, these lesions have the capability to become malignant and metastasize [1]. More importantly, local recurrence is a common issue with phyllodes tumor, occurring in 8-36% of lesions [2]. Rare cases in literature have also noted the event of a phyllodes recurring, but with higher histological grade than the primary tumor [3,4]. Regardless, recurrence arises locally and is widely accepted to be due to lack of negative margins, though cellular and histological traits are still in debate as additive factors [5,6]. Due to these characteristics, surgical excision with wide margins is the accepted mode of treatment for the majority of cases. To our knowledge, there has been no documented case in the literature of a phyllodes tumor occurring serially in a multicentric (multiple quadrants of the ipsilateral breast) pattern as occurred with our patient on more than one occasion.

Case Report

Our patient initially presented as an 18-year-old hispanic female with a single right breast mass in the lower outer quadrant, who was otherwise in good health. Menarche was at 15 years and she

was nulliparous. Family history was negative for ovarian and breast cancer. Ultrasound revealed a 3.1 cm well-circumscribed mass at the 7 o'clock position; based on her age and radiologic findings, this was suspected to be a fibroadenoma (Figure 1). The mass was excised and pathology revealed a 3.0 x 2.5 x 2.0 cm benign phyllodes tumor (Figure 2). We elected to re-excise to achieve wider margins and reduce the risk of local recurrence. Pathology from the re-excision demonstrated clear margins and no residual phyllodes tumor. Two years later, she presented with a right breast mass in the upper inner

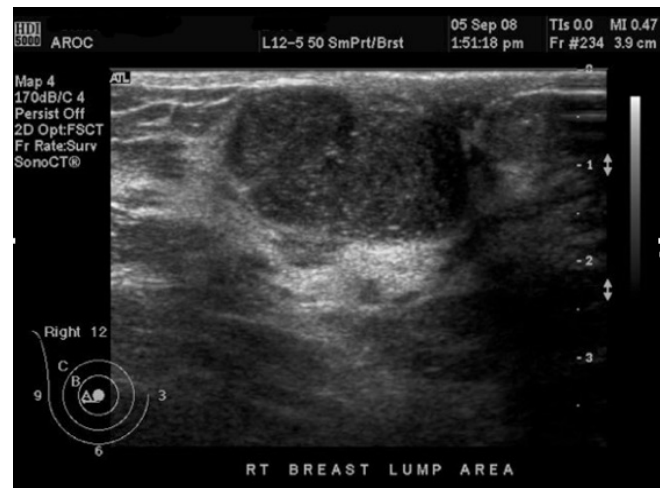


Figure 1: Ultrasound examination demonstrating a 3.1 x 1.7 x 2.5 cm fairly well-circumscribed solid mass at 7 o'clock.

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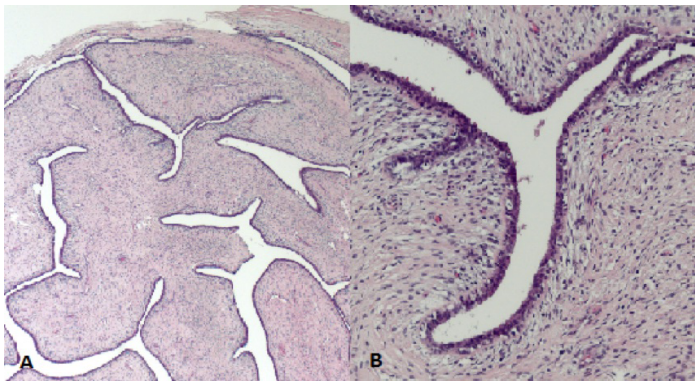


Figure 2: Phyllodes tumor A. Demonstrating leaf-like pattern B. Irregularly-shaped ducts associated with invagination of mildly hypercellular connective tissue

quadrant. Ultrasound demonstrated a 1.85 cm solid mass at the 12 o'clock position suspicious for a fibroadenoma (Figure 3). Due to the patient's history, a core biopsy was performed, which revealed a fibroadenoma with associated normal ductal hyperplasia. The patient underwent resection of the mass that grossly appeared to be a fibroadenoma but pathology determined the specimen to be a 2.0 x 1.5 x 1.0 cm benign phyllodes tumor with positive margins. Again, we elected to re-excise, and pathology revealed no residual tumor.



Figure 3: Ultrasound examination demonstrating a minimally lobulated solid mass measuring 1.85 x 0.90 x 1.39 cm in diameter at the 12 o'clock near position.

At the age of 24, she presented with a new non-tender breast lump, but unlike before, in the upper outer quadrant. Ultrasound showed a 1.3 cm solid mass at the 10 o'clock position (Figure 4). Core biopsy demonstrated a cellular fibroepithelial lesion, favoring a benign phyllodes tumor. A lumpectomy was performed. Pathology found a low grade phyllodes tumor with inadequate margins. Re-excision was performed, and pathology revealed no residual phyllodes tumor. The patient has had no local recurrences or separate occurrences at 10 months after the most recent resection. Additionally, the patient has been instructed to continue to follow up on a yearly basis as well as to perform self-examination in-between.



Figure 4: Ultrasound examination demonstrating a solid mass in the 10 o'clock near position measuring 1.3 cm in diameter.

Discussion

Fibroepithelial lesions are characterized by stromal and epithelial cell proliferation and include both fibroadenomas and phyllodes tumors. While fibroadenomas are fairly common, phyllodes tumors account for <1% of all breast malignancies and only 2.5% of breast fibroepitheloid lesions [3,6]. Moreover, though fibroadenomas are almost indefinitely benign, phyllodes tumors are capable of becoming malignant and metastasize. Phyllodes tumors are also known for their propensity to recur locally.

On breast examination, phyllodes tumor demonstrates nearly equivocal clinical findings to a fibroadenoma. Both typically present as a smooth, multinodular, well-circumscribed, painless, firm mass. These characteristics would make the tumors practically indistinguishable except for a few occasionally minor differences including rapidity of growth and age at presentation. Phyllodes tumor tends to grow more rapidly than a fibroadenoma and presents more commonly at a later age than a fibroadenoma, 42-45 vs 15-35 years of age, respectively [7]. We first believed the lesion in the case we presented to be a fibroadenoma due to our patient's age at presentation and physical exam findings.

Phyllodes tumor and fibroadenoma also share other diagnostic similarities on mammography and ultrasound imaging; both are well-circumscribed, solid and hypoechoic. Minor differences in phyllodes tumors include their heterogeneity with lobulation, and although they are well-circumscribed they typically show irregular margins [8]. Core biopsy is the diagnostic modality of choice and true distinction is made histologically. Phyllodes tumor differs from fibroadenoma by the degree of stromal cellular atypia, mitotic activity, increased stromal cellularity/overgrowth, and the degree of epithelium in the sample. However, benign phyllodes tumors lack marked increased atypia and mitoses when compared to malignant phyllodes [9]. Therefore, a benign phyllodes tumor could be mistaken as a fibroadenoma histologically if only a segment of the tissue is biopsied, as opposed to the entire mass, as

occurred in the second occurrence in our patient. Also, on gross examination distinction is still challenging with both appearing as grayish white multinodular masses.

Commonly accepted treatment for benign phyllodes involves local excision with a minimum of 1 cm margins as to minimize the risk of the characteristic local recurrences [2,10,11,12]. Local recurrence occurs at the site of previous excision, and is the most common location for recurrence. Multifocality, or within the same quadrant of the ipsilateral breast, has been variably reported within literature, but occurs infrequently, with highest incidence noted to be 12% [13]. Similarly, bilateral occurrence is rare with incidence between 0-3.5% [14]. There has been no documented case of a phyllodes tumor reoccurring in a multicentric (within multiple quadrants of the ipsilateral breast) pattern, or occurring serially on three separate incidents, as was the case for our patient. For malignant and borderline phyllodes tumor, there is no clear consensus on whether wide margin excision is sufficient as opposed to mastectomy [5]. The latter has been noted to be the better option for larger tumors where cosmesis may be an issue. Re-excision is recommended for tumors with positive margins after initial excision, stromal overgrowth, and for malignant tumors [15]. Adjuvant radiotherapy after conservative breast surgery may be used for borderline or malignant phyllodes tumor but efficacy is not yet determined, and chemotherapy remains controversial [16,17,18]. For simple fibroadenomas, excision is not necessary and may only be considered for symptomatic relief.

Metastasis occurs in up to 13-40% of cases and most commonly spreads to the lung or pleura (75.1%) [11,17,19,20]. Local recurrence occurs within a few years after surgery and is due especially to incomplete excision [2]. In terms of local recurrence, while positive surgical margins have been documented in literature to be a major contribution to local recurrence in phyllodes tumors, other characteristics, such as tumor size, surgical option chosen, stromal overgrowth, high stromal cellularity, high mitotic rate, etc., hold debating validity [1,3,5,6,22,23]. Since phyllodes tumors are infrequently multifocal, no treatment selection had been determined for the case we presented, which was rather multicentric in pattern of occurrence. Due to the benign nature of the lesion, on each separate occasion in the case we presented, surgical excision with wide margins was performed.

Molecular analysis of phyllodes tumors is also being performed with increasing popularity. Increased chromosomal copy changes have been shown to favor malignant/borderline phyllodes tumors over benign (12.42 & 14.08 vs. 5.58) [25]. Additionally, increased number of chromosomal abnormalities (19 vs. 3.5) has been associated with recurrent/metastatic phyllodes tumors [26]. In particular, Lu et. al. also showed that the gain of chromosomal material in 1q was associated with recurrence, specifically in those without a gain in 1p [27]. Additional chromosomal changes found in malignant/borderline phyllodes tumor include +5p, +7, +8, -6, -9p, -10p, -13 [28]. Mutations to the MED12 gene on chromosome X may also aid in prognosis, as this mutation has been found more commonly in benign phyllodes tumors vs. malignant (65.1% vs.

42.8%) [29,30]. Our patient did not undergo molecular analysis, but may benefit from this in the future as more uniform diagnostic molecular indicators become available.

The distinction between phyllodes tumor and fibroadenoma is sometimes challenging, but is crucial when determining the diagnosis and considering treatments. This was especially true in our case due to the young age of the patient, the vast similarities to a fibroadenoma in regards to physical exam features and radiologic studies, and most importantly serial occurrence in three separate quadrants of the right breast. We recommend that multicentric phyllodes lesions should be considered in patients with a history of phyllodes tumor regardless of subsequent negative biopsies or location of recurrence or occurrence within the breasts. As such, it may be reasonable for patients with a history of phyllodes tumor to undergo wide marginal excision on future breast masses based on the presumption that such masses may be phyllodes tumors.

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