Incidental finding of delayed transformation of fibroadenoma to phyllodes tumor in young female: A Case Report

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ABSTRACT

Phyllodes tumors arising from fibroadenomas are rare occurrences, particularly in young females. We present a case of a 27-year-old woman with a history of benign left breast fibroadenoma, who presented with right flank pain. Initial investigations revealed a significant enlargement of a previously identified benign left breast fibroadenoma. Imaging studies demonstrated a macro-lobulated solid non-calcific lesion, notably larger than before, prompting referral to a breast clinic. Subsequent diagnostic ultrasound and contrast-enhanced MRI revealed a lesion displaying features concerning for phyllodes tumor. Biopsies performed in 2021 and at presentation (2022) indicated a transition from solitary benign fibroepithelial lesion (fibroadenoma) to borderline phyllodes tumor. Surgical excision lumpectomy was undertaken, with histological examination confirming borderline phyllodes tumor, stromal hyperplasia with mild cytologic atypia, and a notable mitotic rate of 9 per 10 high-power fields. This case underscores the importance of vigilance in monitoring fibroadenomas, as they may undergo transformation into phyllodes tumors.

INTRODUCTION

Breast fibroadenomas are frequently encountered benign tumors of the breasts, accounting for approximately two-third of the breast tumors. They are formed due to the overgrowth of glandular tissues primarily caused by hormonal fluctuations during the onset of puberty in girls [1]. Fibroadenomas commonly present as palpable mass that is characterized by proliferation of epithelial and stromal components. Although fibroadenomas may present at any age, they are commonly reported in women between the ages of 14 to 35 [2]. Furthermore, approximately 27.6% cases are reported in women between the ages of 18 to 40 years. The incidence of fibroadenomas dips as age increases, with rare cases reported in post-menopausal women [3]. Although fibroadenomas are benign in nature, they have significant clinical relevance as they mimic malignant tumors. Both fibroadenomas and phyllodes tumors are classified as cellular fibroepithelial lesions. They are also termed as biphasic because they comprise of both stromal and epithelial components. In routine mammography and ultrasound, it is often difficult to distinguish between these two due to similarity in their composition. Phyllodes tumors of the breast are a rare fibroepithelial neoplasm that accounts for less than 1% of all breast neoplasm with incidence rate <0.5 % of all breast lesions [4]. Treatment of fibroadenomas usually focus on regular screening as their size fluctuate depending upon the hormonal pattern. On the other hand, phyllodes tumors are not likely to regress and require surgical approach for their management. Although they are distinct entities with different growth patterns, it is possible for a fibroadenoma to undergo sarcomatous transformation and develop into a phyllodes tumor, but this is a rare occurrence. In this case study, we discuss a female patient who underwent delayed transformation of fibroadenoma to phyllodes tumor.

CASE PRESENTATION

27 years' old women with history of pathology proven benign left breast fibroadenoma presented to the emergency department on November 2021 complaining of right sided flank pain since last 10 days prior to her presentation associated with nausea and vomiting. Initial laboratory investigations and ultrasonography of the upper abdomen were within normal limits. The patient was referred to the urology outpatient clinic and non-contrast CT scan of the urinary system was requested. The computed tomography (CT) scan was unremarkable aside from left breast showing large macro-lobulated solid non-calcific lesion (Figure 1) that was seen and evaluated radiologically in 2016 but the current lesion appeared larger allowing for technical differences, for which the requesting physician was informed and she was referred to the breast clinic for triple assessment and further management. Her clinical examination revealed left breast mass from 4-7 o'clock measuring 60 x 50 mm, which was mobile, not attached to the skin or muscle. No palpable lymph nodes. Diagnostic ultrasound and contrast enhanced MRI of both breast were requested by the breast surgeon.

The B-mode ultrasound was performed using linear 6-15MHz probe [GE Logiq Ultrasound Machine XDClear] revealed left breast irregular well-circumscribed heterogeneously hypoechoic antiparallel lesion, located in the same vicinity of the previously mentioned fibroadenoma, almost doubled in size

measures 62.5 x 37.8 x 58.5 mm [previously in 2016: 29 x 23 x 28 mm] with newly noted mild surrounding edema, increased surrounding and internal vascularity on color doppler. The lesion was seen at ~31 mm from nipple, abutting the overlying skin with no evident direct invasion nor skin thickening, no nipple retraction, no calcification, no lymphadenopathy, no other surrounding lesions (Figures 2,3). The same lesion was biopsied in 2021 and proven benign fibroepithelial lesion (b2) favoring fibroadenoma. Global sonographic screening for both breast revealed no other lesions.

The accompanied contrast enhanced MRI of the breast [performed on siemens Achieve 3T magnet, with T1, T2 sequences, Diffusion weighted images, fat suppressed dynamic sequences following gadolinium by patient weight] was done, eliciting left breast lesion showing low T1, high T2 signal intensity with variable degree restricted diffusion more seen at its inferio-anterior parts, heterogenous post contrast enhancement and multiple internal non-enhancing dark septations, displaying type I kinetic curve, few indeterminate left axillary lymph nodes were also noted (Figures 4) The patient again underwent ultrasound guided core biopsy with 16 G needle of the lesion with histopathology results of borderline phyllodes tumor.

The patient underwent surgical excision lumpectomy with uneventful perioperative and postoperative hospital stay. Definitive histology showed Borderline Phyllodes Tumor, stromal hyperplasia with mild cytologic atypia, mitotic figures 9 per 10 HPF, back ground breast parenchyma shows sclerosing adenosis (Figure 5).

DISCUSSION

In 1838, Johannes Muller coined the term "phyllodes tumor" or "cystosarcoma phyllodes" to describe non-epithelial breast tumors. However, the term "cystosarcoma phyllodes" has been reconsidered because it may not be entirely appropriate, as 35–64% of phyllodes tumors are benign, rendering the inclusion of "cystosarcoma" misleading [5]. The etiology of phyllodes tumor is well understood, typically affecting adult women aged 33 to 55. Histopathologically, it comprises a stromal component surrounded by epithelium, giving it a leaf-like appearance. The World Health Organization (WHO) categorizes the disease into three types: benign, borderline, and malignant, based on various factors including tumor margins, mitotic activity, cellular stroma, atypia, and stromal growth. Another classification by Azzopardi and Salvadori considers tumor margins, cellular stroma, mitotic count, and presence of pleomorphism [6,7]. The transformation of fibroadenomas into phyllodes tumors is uncommon, but it can happen when recurrent FAs grow excessively.

This transformation typically occurs more frequently in individuals before menopause. Malignant Phyllodes tumors, originating from mesenchymal tissue, exhibit behaviors akin to sarcomas. Around 10–20% of these tumors metastasize hematogenously, commonly affecting the lungs, bones, and liver. Due to their propensity for local recurrence, borderline Phyllodes tumors are managed surgically with subsequent radiotherapy similar to malignant cases [8,9]. The efficacy of chemotherapy for borderline or malignant phyllodes tumors remains a subject of debate. Certain studies suggest that chemotherapy may not significantly impact survival rates for these tumors [10]. However, there are indications that chemotherapy, particularly using regimens such as epirubicin and ifosfamide commonly employed for sarcomas, can yield positive outcomes, especially for malignant phyllodes tumors that have extensively metastasized. In some instances, distant metastases have been successfully eradicated. Moreover, in cases where neoadjuvant chemotherapy was administered, there have been instances where it led to a reduction in tumor size by over 50% [10,11].

In our case, the patient presented first with left breast mass for which she underwent an ultrasound breast showing a solitary lesion which had a biopsy proven fibroadenoma that transformed after six years to Borderline phyllodes tumor. The likelihood of misdiagnosis from the first biopsy is less likely since the mass was stable in size and appearance from 2016 until 2021 with no other lesions seen in the breast. However, due to overlapping histological features differentiating the lesions is difficult. Previous cases showed post excision of pathology proven fibroadenoma breast lesion transforming to borderline phyllodes tumor over a one-year time period [12], another case developed a malignant phyllodes tumor from a fibroadenoma in three years [13] and post partial mastectomy of fibroadenoma with malignant phyllodes tumors transformation [14]. Despite the similarities between these cases and the one presented in our case report, one interesting point should be noted about the timeline over which these masses developed. To the best of our knowledge, we believe our case to be the longest time-lapse (8 years) for the conversion of a fibroadenoma into a phyllodes tumor.

Recent studies have investigated how fibroadenomas may progress into phyllodes tumors, offering clinicians insights to foresee potential transformations. Genetics stands out as a promising avenue, given the known associations of phyllodes tumors with conditions like Li-Fraumeni syndrome and BRCA1/2 mutations [14]. Recent studies have identified common mutations associated with both fibroadenomas and phyllodes tumors, notably in genes like MED12 exon 2, TERT promoter, and RARA [15]. These genes play crucial roles in DNA synthesis regulation, and mutations in them can trigger uncontrolled cell growth, a hallmark of these breast lesions. One study devised a 16-gene panel, including MED12 exon 2, TERT promoter, and RARA, as a diagnostic tool for characterizing fibroepithelial lesions in the breast. Analyzing 275 breast specimens, Sim et al. found that MED12 exon 2 mutations were prevalent in both fibroadenomas and phyllodes tumors across all grades, suggesting a biological connection between them. Moreover, they observed a significantly higher mutation rate of TERT promoter and RARA genes in phyllodes tumors compared to fibroadenomas. Thus, they proposed their 16-gene panel could aid in distinguishing between these lesions on core biopsies [16].

Some authors have highlighted the added value of high-frequency sonography for the finest superficial breast parenchyma spatial resolution and anatomical details [17]. For breast sonography examination, two multi-frequency linear probes can be used. The first probe, with a frequency range of 7.5 to 14 MHz, is recommended by the American College of Radiology due to its superior penetration, allowing for the examination of deeper layers such as the muscle plane, fascia, and retromammary layer, as well as larger lesions. The second probe, with a frequency range of 15 to 24 MHz, is essential for its higher resolution, making it suitable for scanning superficial planes [18]. Although not used in the present study, it can be used in cases similar to ours. Rjosk-Dendorfer et al. reported that use of color Doppler breast sonography at 17 MHz allowed for the differentiation of cysts from solid masses compared with 12.5 MHz. However, this increase in frequency did not enhance the ability to distinguish between benign and malignant masses [19]. Furthermore, the use of strain elastography in differentiating benign and malignant breast lesions based on their stiffness has also been documented [20].

CONCLUSION

In conclusion, this case presents a rare incidental finding of delayed transformation of fibroadenoma to phyllodes tumor in a young female. The patient initially presented with right flank pain, prompting evaluation that incidentally revealed significant enlargement of a previously diagnosed benign fibroadenoma. Subsequent imaging and biopsies confirmed the presence of a borderline phyllodes tumor, demonstrating stromal hyperplasia with mild cytologic atypia. The management involved surgical excision lumpectomy, which proceeded without complications. This case underscores the importance of vigilant monitoring of benign breast lesions, particularly in young individuals, as they may undergo malignant transformation over time.

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FIGURES

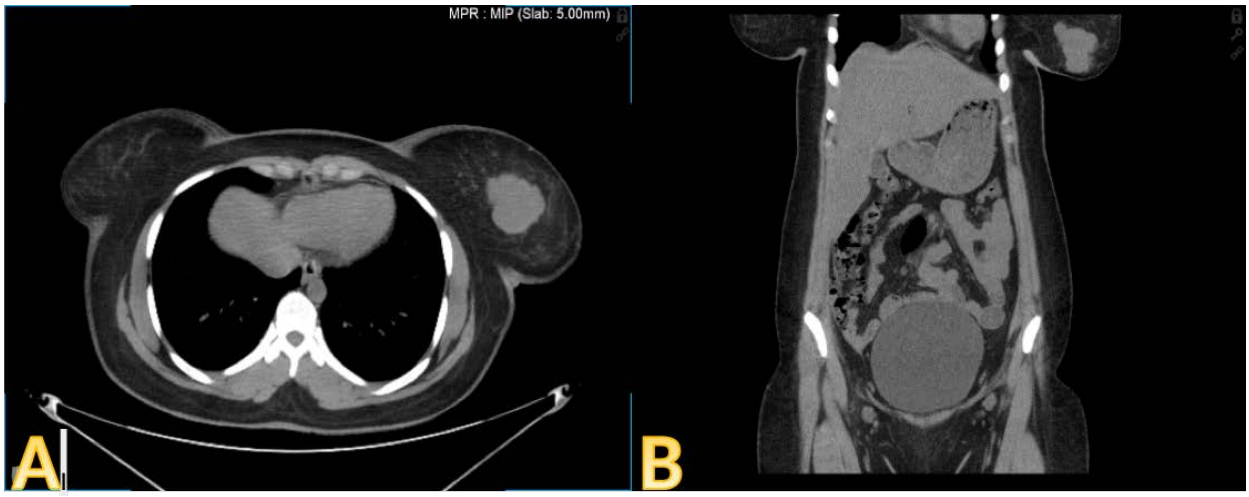

Figure 1: Non-enhanced computed tomography (CT) scan of the abdomen and pelvis in axial (A) and coronal (B) plains showing: left breast lower mid quadrant large well-defined multiloculated hypodense lesion with no dense calcification, no fat component, no skin thickening, no surrounding invasion.

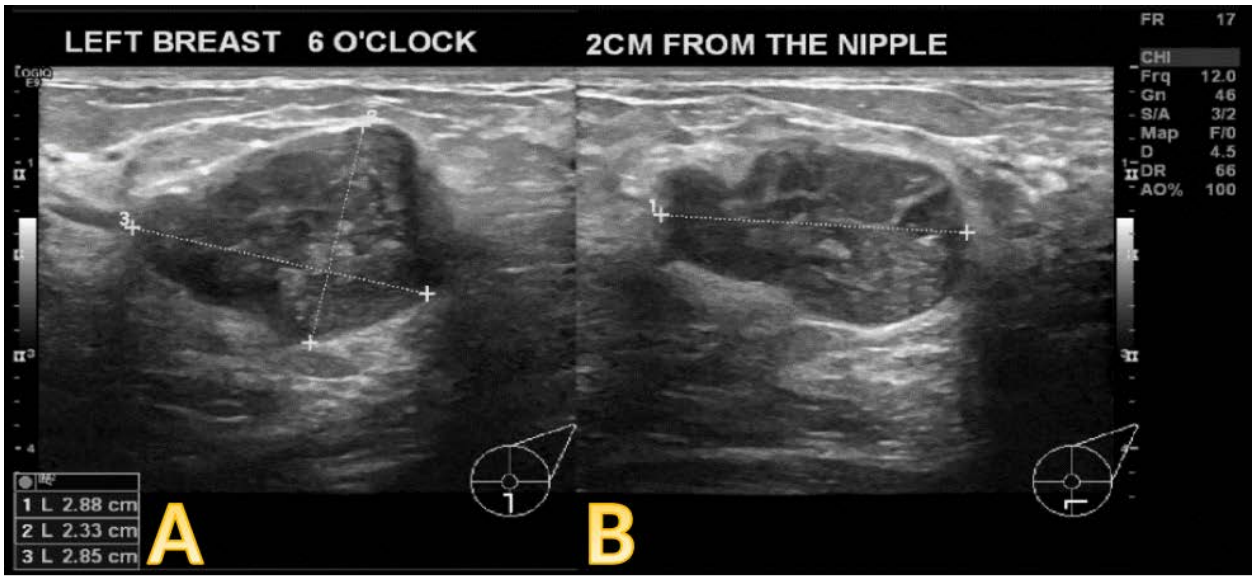

Figure 2: B-mode ultrasound of the left breast showing breast composition of heterogenous background echotexture ACR C, showing solitary solid lesion located in the mid lower quadrant at 6 o'clock, 2 cm away from the nipple, irregular in shape, circumscribed margins, parallel orientation, with heterogeneous echopattern predominantly hypoechoic, posterior acoustic enhancement, no increased vascularity on color doppler (images not provided).

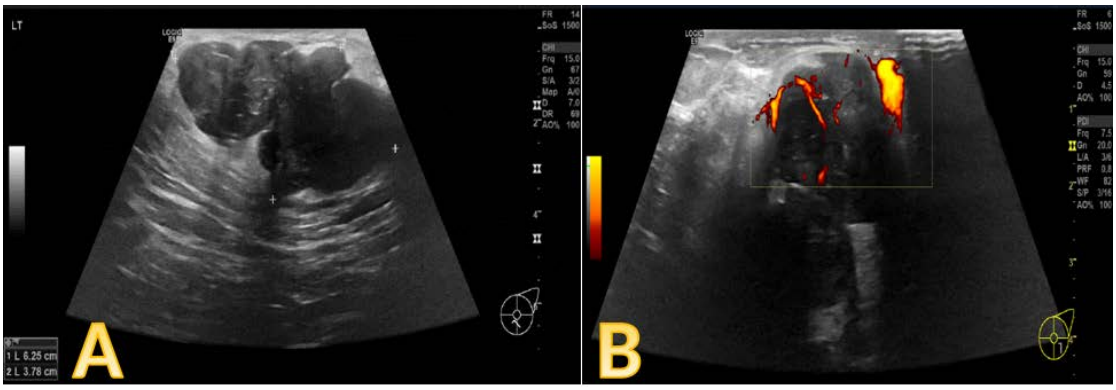

Figure 3: B-mode and doppler ultrasound of the left breast after 5 years showing interval progression of the previously described lesion appearing as: large Solid mass, irregular in shape with anti-parallel orientation, angular margins, heterogeneously hypoechoic with posterior acoustic enhancement, no calcification, increased internal vascularity on color Doppler (B). No overlying skin changes or pathological lymphadenopathy.

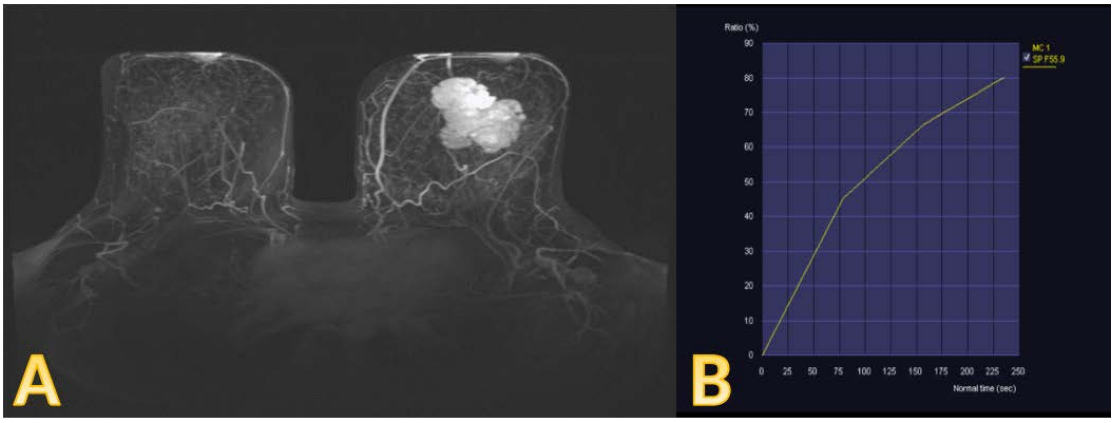

Figure 4: Contrast-enhanced Magnetic resonance imaging (MRI) of both breasts in maximum intensity projection (MIP) sequence showing bilateral mild background parenchymal enhancement of both breasts, solitary left breast large irregular mass with circumscribed margins showing homogeneous postcontrast enhancement, no overlying skin changes, no nipple retraction (A). type I enhancement curve: progressive or persistent enhancement pattern (B).

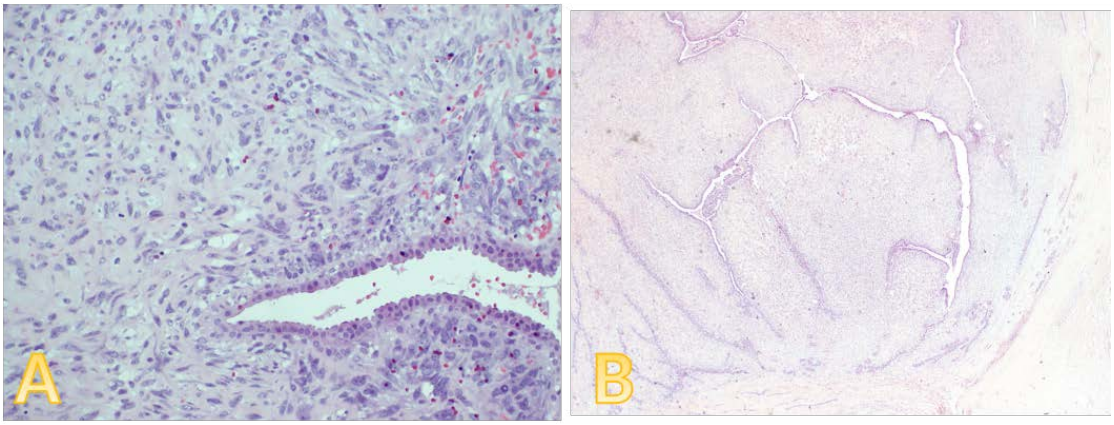

Figure 5: Histopathology Hematoxylin and Eosin (H&E) staining showed: stromal hypercellularity with mild cytological atypia and increase in mitotic figures (A), whereas the right side image is showing circumscribed lesion composed of stoma and benign glandular elements with intracanalicular pattern.

KEYWORDS

Fibroadenoma, Phyllodes Tumor, Breast Lesion, Benign, Malignant Transformation