

## Recurrent Bilateral Giant Fibroadenomas of the Breasts

Ashley Morris, B.S., and Kitt Shaffer, M.D., Ph.D.

We present a case of an 18-year-old woman with recurrent bilateral giant fibroadenomas that were evaluated by mammography and sonography with color Doppler. Imaging revealed solid lobulated masses with significant internal vascularity occupying most of each breast; this evaluation suggested a differential diagnosis of giant fibroadenoma versus phyllodes tumor. The unusual clinical story of recurrent bilateral lesions as reported by the patient, coupled with the findings on visualization of these lesions by mammography and ultrasound with color Doppler, led to the clinical decision to forego biopsy in favor of immediate bilateral surgical enucleation.

### Introduction

The term “giant fibroadenoma” is a descriptive name given to a fibroadenoma that is greater than 5cm in diameter or weighs more than 500g [1]. These rare benign tumors most commonly affect females of Afro-Caribbean or East Asian descent and have a bimodal age distribution with occurrence typically either in adolescent or premenopausal women [2]. Giant fibroadenomas can be variants of either adult type fibroadenomas or the less common juvenile fibroadenoma, both of which are benign circumscribed breast masses resulting from proliferation of stromal and

epithelial (glandular) tissue [3]. In this report, we present the case of recurrent bilateral giant fibroadenomas in an 18-year-old female from Haiti. The subsequent discussion addresses those features of this case that are typical of this diagnosis, as well as the unique aspects of this specific clinical presentation.

### Case Report

An 18-year-old female from Haiti presented to the Cambridge Hospital Breast Center with a chief complaint of bilateral painful, swollen breasts for the past 1.5 years. On further history she explained that she had originally experienced a burning pain in both breasts exclusively around the time of menstruation but that this pain had since become constant. She remarked that the increased frequency of the pain correlated with a marked gradual increase in size of both breasts over the course of the past two years. She denied any change in breast size with menses, any nipple discharge, or any constitutional symptoms. The patient did note that she had similar “lumps” surgically removed from both breasts approximately 2.5 years prior to this current presentation, at the age of 16, while still living in Haiti; she reported that at the time of the prior surgery she was informed that the lumps were cysts. She stated that subsequent to the previous surgery her breast size was sig-

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Abbreviations: BI-RADS, Breast Imaging Reporting and Data System; FNA, fine needle aspiration; MRI, magnetic resonance imaging

Ashley Morris (Email: ashley\_morris@hms.harvard.edu) is at Harvard Medical School, Boston, MA, USA.

Kitt Shaffer, M.D., Ph.D. (Email: kshaffer@challiance.org), is in the Department of Radiology, Harvard Medical School and Cambridge Health Alliance, Cambridge, MA, USA.

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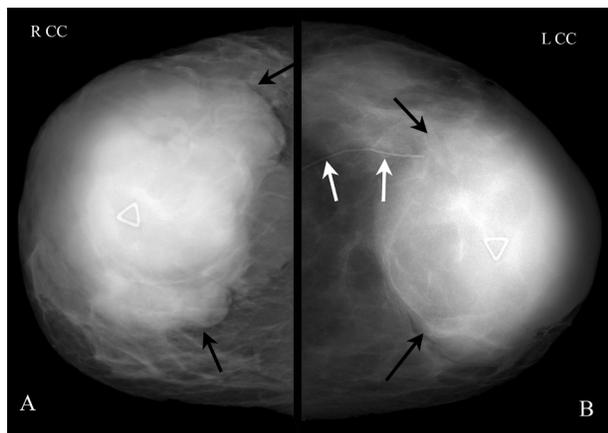


Figure 1A. 18-year-old woman with recurrent bilateral giant fibroadenomas. Mammographic craniocaudal views of both breasts show large, dense, homogeneous masses (black arrows) approximately 12 cm at its largest diameter on the right and 10 cm on the left. A skin marker noting the site of prior surgical scar is indicated by the white arrows.

nificantly reduced but that her breasts soon began to grow again and that currently both were much larger than they had been at the time of the first procedure. She originally attributed this growth to normal development and only sought medical attention when the associated pain became unbearable.

The patient was screened for known breast cancer risk factors. She reported menarche at age 12 without consequent use of oral contraception and denied any pregnancies. The patient denied any alcohol use or previous radiation exposure. She was not taking any medications. Her only pertinent family history was a maternal great aunt who had breast cancer in her 50s.

On physical exam at the Breast Center the patient was found to have visibly distorted breast contours bilaterally. On palpation, the right breast was found to be occupied by a large, irregular, hard protuberant mass that filled most of the breast. This was accompanied by overlying shiny, thinned skin with several prominent dilated veins, likely due to the proximity of the mass to the skin. The left breast was similarly occupied by a large, irregular, hard protuberant mass in the central region, smaller than on the right and without any overlying skin changes. The patient did not have any evidence of nipple abnormalities or axillary lymphadenopathy.

The patient was sent for bilateral mammograms and ultrasounds of the lesions, with concern of slow growing sarcoma or phyllodes tumor. Mammography showed highly suspicious large homogeneous lobulated masses

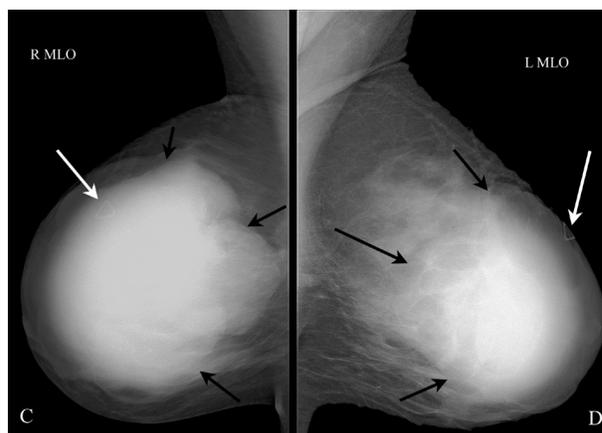


Figure 1B. Mammographic mediolateral oblique images of the right and left breasts show large masses (black arrows). Skin markers are present at the white arrows, indicating palpable abnormalities.

occupying most of each breast. The lesion on the right was approximately 12 cm in diameter while that on the left was approximately 10 cm in diameter (Fig. 1). Neither mass appeared to extend to the pectoralis muscle and there was no evidence of suspicious calcification in either breast.

Breast sonography demonstrated fairly homogeneous hypoechoic solid lobulated masses occupying most of each breast, with internal vascularity demonstrated by color Doppler and increased through transmission (Figures 2A-D). The imaging studies of the breasts were together classified as BI-RADS 5: highly suggestive of malignancy with indication for biopsy.

Given the alarming history of the rapid recurrence of these tumors and the striking vascularity indicated by ultrasound of the lesions, it was decided that biopsy would not change the management of the patient's case and could potentially introduce complications such as bruising, bleeding, infection or pain. Furthermore, neither fine-needle aspiration biopsy nor core needle biopsy has been found to be efficacious in the differentiation between phyllodes tumor and fibroadenomas. Rather, surgical intervention was indicated. The patient was taken to the operating room where she underwent bilateral enucleation of the breast masses (Fig. 3). The surgical specimens were sent to pathology where histologic examination concluded a diagnosis of benign giant fibroadenoma variants (Fig. 4).

### Discussion

Fibroadenomas are the most common cause of a breast mass in young females, accounting for approximately 75%

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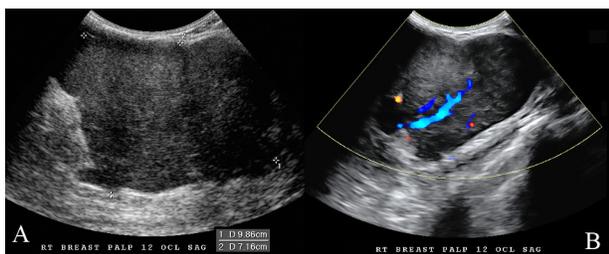


Figure 2A. Sonography of the right breast shows a large solid lobulated hypoechoic lesion occupying most of the breast. Color Doppler study of the right breast mass reveals significant intralesional blood flow.

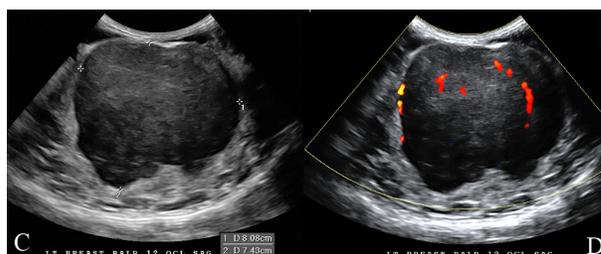


Figure 2B. Sonography of the left breast showing a large solid hypoechoic lesion, slightly larger than that on the right, occupying most of the breast. Color Doppler study of the left breast mass reveals significant intralesional blood flow, similar to that found in the right breast lesion.

of all breast lesions in young females [4]. However only 0.5-2% of all cases of fibroadenomas can be classified as giant fibroadenomas [5]. Furthermore, the development of multiple fibroadenomas, as presented in this case, occurs in only 15% of cases of giant fibroadenomas [6]. As a teenaged female of Afro-Caribbean descent, the patient depicted in this case represents the “classic” patient afflicted with this rare condition.

Giant fibroadenomas typically present clinically with pain and breast enlargement. They are usually smooth, firm, nontender and mobile to palpation, and most often occur in the upper outer quadrant of the breast [7]. There may be overlying skin changes. Other potential causes of significant breast enlargement, or macromastia, which must be considered when evaluating a patient presenting with this complaint include juvenile hypertrophy, macrocyst, lipoma, hemangioma, pseudoangiomatous stromal hyperplasia, cystosarcoma phyllodes and fibroadenoma. A thorough history and physical exam, coupled with appropriate imaging evaluation, allows for narrowing of the differential. Juvenile (benign virginal) hypertrophy is a rare condition caused by an abnormal response to estrogen resulting in tissue hypertrophy, either unilaterally or bilaterally. This condition is not associated with the presence of a definable mass lesion on physical or imaging evaluation [5]. Macrocysts may present with both pain and breast enlargement, however on ultrasound these masses will appear as anechoic, fluid-filled lesions [8]. The mass lesion caused by a lipoma will be soft and is typically neither mobile nor discrete, while a large hemangioma would typically have associated cutaneous signs of vascular proliferation. Pseudoangiomatous stromal hyperplasia (PASH) is a rare condition which usually presents as small incidental foci or tumors in premenopausal women, rather than large nodular masses in young women, with only 4 documented

cases of the latter presentation. Thus, while the categorical exclusion of PASH as a diagnosis requires histologic examination, it remains epidemiologically an extremely unlikely diagnosis [9]. Therefore despite the multiple diagnoses that must be considered with such a presentation, most diagnoses have specific clinical or imaging features that distinguish them. However, there is no such distinguishing clinical or imaging feature that discriminates between cystosarcoma phyllodes and giant fibroadenoma, and thus determination of a final diagnosis is particularly challenging.

The appearance of a giant fibroadenoma on mammography is consistent with that of a benign fibroadenoma: a dense, sometimes lobulated, well-circumscribed mass with sharp margins. There may be a surrounding lucent halo. However, since giant fibroadenomas most commonly occur in pre-menopausal women, the pathognomonic “popcorn-like” calcifications that may be appreciated on mammographic imaging of fibroadenomas are rare in giant fibroadenomas, since this finding results from involution of the tumor in post-menopausal women [6].

The mammographic findings in the presented case were designated BI-RADS 5, implying a likelihood of malignancy greater than 95%. However, several features of the clinical presentation and imaging findings pointed to a benign process, suggesting that BI-RADS 4 might have been a more suitable designation. Specifically, the masses were smoothly margined, bilateral, and occurred in an 18 year old individual. Even if such findings could not exclude the possibility of phyllodes tumors, the majority of phyllodes tumors are benign. Thus, categorizing these mammographic findings as BI-RADS 4, indicating a highly suspicious abnormality with a likelihood of malignancy between 23% and 34% [10], would have perhaps been more appropriate.

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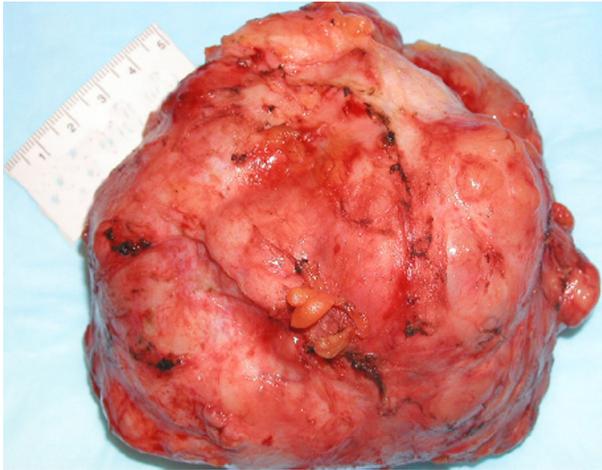


Figure 3A. Gross image of resected right breast mass which measured 11.5 cm by 11 cm by 7 cm. Image courtesy of Dr. Eva Patalas, Cambridge Health Alliance, Dept of Radiology, Cambridge, MA

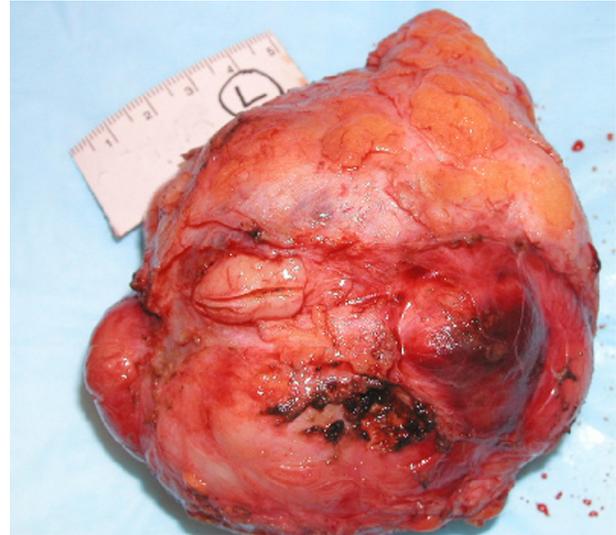


Figure 3B. Gross image of resected left breast mass which measured 10 cm by 10 cm by 7 cm. Image courtesy of Dr. Eva Patalas, Cambridge Health Alliance, Dept of Radiology, Cambridge, MA.

Breast ultrasound allows for discrimination of breast cysts, which are typically anechoic fluid-filled spheres, from solid tumors, which are typically hypoechoic [8]. Specifically, on ultrasonographic evaluation, fibroadenomas appear as well-circumscribed elliptical homogeneous masses that are either hypo- or isoechoic, with smooth borders and posterior acoustic enhancement. They are typically larger in the transverse than the anteroposterior axis [6]. Ultrasound is particularly useful in evaluation of fibroadenomas since young women commonly have dense breast tissue, rendering mammography more difficult. While the presence on ultrasound of clefts or cysts in a well-defined solid mass is typical of a phyllodes tumor, this is not a pathognomonic findings and further diagnostic evaluation is mandatory. [11]

MRI is currently emerging as a useful complement to the more established breast imaging modalities. On T2-weighted images of fibroadenomas, septations which demarcate the separation between lobules can be appreciated. This pattern emerges because of the characteristic growth of fibroadenomas in adjacent lobules [5]. This feature alone, however, is not sufficient to distinguish between a phyllodes tumor and a giant fibroadenoma. Thus, even with the addition of MRI to the radiologic armamentarium, imaging survey and clinical examination do not provide adequate information for the conclusive diagnosis of giant fibroadenoma.

A giant fibroadenoma can be distinguished histologically from a phyllodes tumor by the lack of stromal atypia,

stromal overgrowth, stromal condensation surrounding ducts, and leaf-like architecture typical of a phyllodes tumor (Figure 4A, 4B) [12]. Rather, a giant fibroadenoma will have histology consistent with that of a fibroadenoma: a well-circumscribed proliferation of stromal and epithelial tissue, which can be classified as pericanalicular, intracanalicular, or variant, referring to the location of the stromal proliferation. This subclassification is a histologic distinction and carries no prognostic value. The distinction between phyllodes tumor and giant fibroadenoma, however is prognostically significant: phyllodes tumors may be malignant while fibroadenomas are benign, with no association between the presence of a fibroadenoma and subsequent breast cancer development [13]. Though benign, because of their size giant fibroadenomas are nonetheless associated with significant morbidity, including venous congestion, glandular distortion, pressure necrosis, and occasionally ulceration [5, 14].

Of note, there is a documented association between the use of cyclosporine A therapy in renal transplant recipients and the occurrence of multiple fibroadenomas. Specifically, several cases of multiple giant fibroadenomas in association with cyclosporine A therapy have been reported. Possible mechanisms to account for this effect include direct effects of cyclosporine A on fibroblasts of the breast tissue, antagonism of prolactin receptor sites, effects on the hypothalamic-pituitary axis, and resolution of uremia [11,

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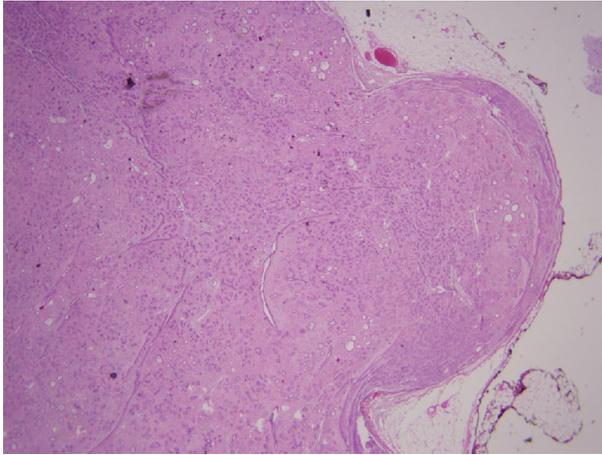


Figure 4A. Low-power histologic examination of the right breast mass reveals a well-demarcated lesion characterized by fibroepithelial proliferation. Image courtesy of Dr. Eva Patalas, Cambridge Health Alliance, Dept of Radiology, Cambridge, MA.

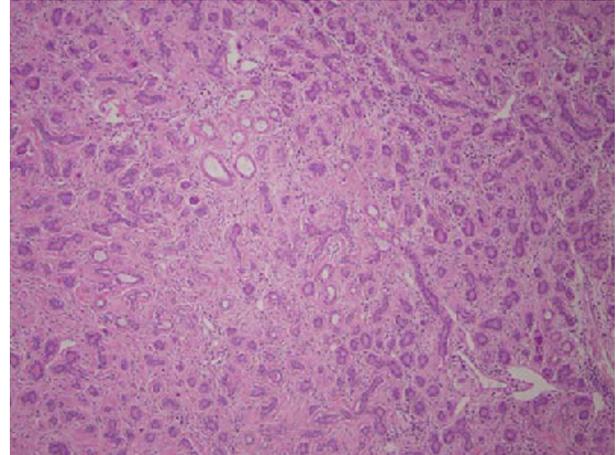


Figure 4B. High-powered photomicrograph of the same mass shows elongated, compressed ducts (black arrows) as well as some dilated ducts (white arrows). Note the lack of architectural features typical of a pericanalicular or intracanalicular fibroadenoma, leading to classification of this lesion as a fibroadenoma variant. Image courtesy of Dr. Eva Patalas, Cambridge Health Alliance, Dept of Radiology, Cambridge, MA.

15]. Though a well-recognized side effect of cyclosporine A is increased incidence of malignancy, the incidence of de novo breast cancer in women who are chronically immunosuppressed following transplant is lower than that of the general population, and thus development of fibroadenomas in association with cyclosporine A therapy should not raise increased concern for malignancy [1]. Resolution of the fibroadenomas upon cessation of cyclosporine A therapy has been observed in one case, however more commonly the breast masses persist unchanged in size or appearance.

The management of a giant fibroadenoma differs from that of a phyllodes tumor. Typical surgical intervention for a fibroadenoma is enucleation, while excision with wide margins is the standard of care for a phyllodes tumor [16]. However, there is no definitive means of distinguishing between these two possible diagnoses without pathologic examination of the entire specimen. Thus, surgeons are left with a conundrum: a decision regarding surgical approach must be made prior to the ascertainment of the diagnosis on which such a decision should be predicated. Specifically, neither fine-needle aspiration (FNA) nor core biopsy has been proven efficacious in the definitive diagnosis of a phyllodes tumor, since the microscopic heterogeneity of both lesions introduces significant sampling error to these more conservative diagnostic approaches. Cytological features of specimens from FNA biopsy, such as hypercellular stromal fragments, can be present in both phyllodes

tumors and fibroadenomas. Multinucleated stromal giant cells are less common in fibroadenomas than phyllodes tumors but considered non-specific and cannot be used as a diagnostic criterion [16]. Histologic features of a sample garnered from core needle biopsy similarly can be interpreted as consistent with either a phyllodes tumor or a fibroadenoma.

In the presented case, both fine-needle aspiration and core needle biopsy were foregone because of the known diagnostic limitations noted above. Rather, an intraoperative decision to enucleate the masses was made following assessment of the size of the lesions and the lack of adequate surrounding tissue margins. It was anticipated that if the specimens were found to be malignant, the patient would be brought back to the operating room for a complete bilaterally mastectomy.

It is the combination of meticulous history taking, an attentive physical exam, a thorough imaging survey, and microscopic pathological examination, which will allow for tailored and definitive care to be delivered to adolescent women presenting with large breast masses. In this young age group, avoiding overly invasive diagnostic and management practices is particularly important. It is the duty of those clinicians caring for such women to strive to address this chief complaint in a manner sensitive to the

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needs and concerns of this demographic. Knowledge of the limitations of traditional diagnostic modalities such as fine-needle aspiration and core-needle biopsy contributes to the ability to deliver such sensitive care. This case serves as an excellent example of a scenario in which the use of multiple radiologic modalities, coupled with a thorough clinical exam, allowed for elimination of unnecessary procedures in favor of the most direct surgical intervention with minimal delay. While fine-needle aspiration could have been performed, the results of this procedure would not have been definitive. Core needle biopsy would have carried significant risk of bleeding, as demonstrated by the substantial vascular structures encompassing the breast masses, and similarly would have been of limited diagnostic value. In this case, expedient and definitive care was delivered through the proper integration of clinical and radiologic findings and the application of these findings to the development of a rational, individually tailored, and ultimately curative surgical intervention.

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