Benign Phyllodes Breast Tumor: Regarding a Young Woman’s Clinical Case

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Abstract

Phyllodes tumors are rare fibroepithelial lesions that count for 0.3-1% of all primary breast tumors. Telling the difference between phyllodes tumors and giant juvenile fibroadenomas, that rarely affect adolescent and young women, is difficult but of importance because resection with margins is the mainstay of treatment for phyllodes tumors.

We report a clinical case of an eighteen-year-old female patient, with past history of left breast lump excision four years before, classified as “juvenile fibroadenoma”.

In early 2015, she was referred to the consultation by the appearance of a bulky ipsilateral lump (10.8 x 6.9 cm), core-biopsy histology revealed “fibroadenoma with more lax stroma vs benign phyllodes tumor”. Surgical excision of the lesion was performed.

Histology of the specimen confirmed “benign phyllodes breast tumor (14 x 12 x 8 cm and 788 g)”. Given its benign nature and negative margins, the patient did not require further treatment and currently attends in follow-up consultation.

A brief discussion of this rare form of fibroepithelial tumor, minding its classification, diagnosis, treatment, follow-up and prognosis is done.

Keywords: Benign phyllode tumor; Juvenile fibroadenoma; Fibroepithelial lesion; Clinical case report

Brief Thematic Review

Breast phyllodes tumors (PT) and fibroadenomas (FA) are fibroepithelial lesions that represent a heterogeneous group of biphasic lesions with proliferation of both stromal and epithelial components. They present clinical and imaging similarity as nodular lesions, not reliably distinguishable, although some specific ultrasound (US) characteristics, such as internal fluid areas or hyperechoic septa, may be seen in some PTs [1,2].

Phyllodes tumors

The name “phyllodes” derives from the Greek words phyllos (leaf) and eidos (form). Phyllodes tumor was first described in 1838, by Johannes Müller, using the name “cystosarcoma phyllodes”, referring to its malignant potential. Many other synonyms are found in the literature and so, in order to make terminology and criteria uniform, the World Health Organization (WHO) called it as “phyllodes tumor” in 1981 [3].

PTs are rare lesions that represent 0.3%-1.0% of breast tumors and 2%-3% of fibroepithelial lesions [1-8].

Particularly rare in young women, they may occur at any age, being the median age of occurrence between 40 and 50 years [1,2,5,6], but when occurring in young patients it can provoke profound psychological and physical impairment from breast deformity, making prompt treatment mandatory [9].

The WHO classified PTs as benign, borderline, or malignant on the basis of a combination of histological features including the degree of stromal hypercellularity, mitotic activity and cytological atypia of stromal component, stromal overgrowth and nature of the tumor margins-sometimes displacing or infiltrating surrounding tissue and often showing signs of hemorrhage and ulceration [1,2,4,5,6]. Stromal overgrowth and tumor necrosis are considered prognostic factors [5].

Despite the WHO classification, these tumors rarity limits the understanding of its characteristics and prognosis [1,6]. Benign PT incidence is between 35% and 64% while malignant PT accounts for 25% of cases [5]. In general, borderline or malignant PTs can both recur and develop hematogenous metastases, whereas benign PTs can recur but do not metastasize [1,6].

Fibroadenomas

FAs are defined as benign breast lesions, usually appearing after menarche, mostly between 15 and 25 years of age, they can exist as a
solitary mass or multiple masses, usually presenting as unilateral breast masses, accounting for 50–60% of all breast lesions in adolescents [10,11]. On physical examination, these masses may feel like a marble with rounded borders being mobile but hard [10].

Fibroadenomas that measure more than 5 cm are known as giant fibroadenomas, and when they are found in adolescent female patients, they are called juvenile fibroadenomas (JF) and are characterized by a rich cellular stroma and a prominent glandular epithelium. JFs are rare, generally asymptomatic, firm, smooth and mobile, accounting for only 0.5% of the total diagnosed fibroadenomas, and can grow to large sizes and cause prominent asymmetry of the breasts and can lead to stretching of the areola complex and distortion of the skin [9-11].

Differential diagnosis

PTs are rapid growing tumors, and a palpable lump is the most usual manifestation. The initial investigation of a palpable breast lump starts with physical examination and imaging studies which are mandatory, then biopsy. Core-biopsy (CB) is the technique of choice, however, differential diagnosis between benign or borderline PT and FA is specially challenging with core-biopsy (CB) due to the small samples and to the fact that stromal hypercellularity may also be present in JF. Few studies have reported diagnostic accuracy of CB in the diagnosis of PT [1,4,6,12].

According to the European Reporting Guidelines, in situations in which a CB presents a fibroepithelial lesion with increased stromal cellularity, little or moderate stromal cellular pleomorphism and infrequent mitotic figures and distinction between benign/borderline PT and cellular FA is not feasible, the report of the sample should mention “PT” and classified as “B3-lesion of uncertain malignant potential” [1,6,9,12].

Malignant PT are usually easier to identify on CB because of its marked stromal cellular atypia, increased mitotic activity and stromal overgrowth, belonging to the B5 category [1].

Management

Accurate diagnosis of PT nature through preoperative CB is of much importance to allow developing the correct treatment decisions [8].

FAs are benign lesions that can be managed by surgical enucleation or clinical and US follow-up [1,5]. Some newer, less invasive techniques are starting to be used for smaller fibroadenomas, such as ultrasound-guided percutaneous vacuum-assisted excision and in situ cryoablation. These promising approaches are safe and cost-effective when compared with the classical surgical excision, other advantages include faster recovery and better cosmetic results as incisions are minimal. Initial experience tells us that these are both low-risk techniques, apparently more appropriate for older patients with smaller FAs and should be performed by physicians skilled in breast ultrasound [10].

When dealing with JFs no spontaneous regression is expected, by the contrary, they tend to grow very rapidly in size during adolescence, and the attitude should be different from other FAs, so enucleation should be carried out. As malignancy is of lesser concern, esthetics and lactation preservation are the main concerns when excising these lesions [10].

The treatment of choice for phyllodes tumors is surgical excision. The extent of surgery remains controversial. When the preoperative diagnosis is known, the usual recommended treatment for benign PTs is complete surgical excision with free margins. The margin thickness for benign PTs is still controversial, some authors defend a complete surgical resection with histologic negative margins, others recommend a more than 1 mm margin, and others agree on a margin greater than 10 mm [13].

Wide excision is necessary in borderline and malignant tumors because of their higher local recurrence rate and tendency for systemic metastasis [8,14]. Sometimes mastectomy is required in these two former situations [6]. Other authors recommend wide surgical excision with a margin of surrounding healthy tissue for all PTs, including benign PT, to minimize the risk of local recurrence [1,4,5,7].

Axillary lymph node dissection is not usually recommended because malignant phyllodes tumors mainly spread through hematogenous route rather than a lymphatic route [8].

The potential role of adjuvant radiotherapy (RT) in preventing recurrence in borderline and malignant PT is still debated as only a minor fraction of patients have received this treatment. RT seems to reduce the risk of local but not of distant relapse in malignant tumors. In addition, there is an absence of large prospective trials, and so, at this time, RT indication should be limited to patients with malignant tumors and positive surgical margins when a surgical radicalization cannot be done [5,14].

Adjuvant chemotherapy is even more questionable and currently not indicated [5].

Outcome

Prognosis is excellent for both benign and borderline PTs. Not all, but most of the malignant PTs also have a good prognosis if treated correctly with adequate surgery with clear margins. Optimistically, in the near future, molecular characterization may provide valuable information and eventually permit to identify new agents to be used in targeted treatments, for those rare tumors with poor prognosis [5].

Next, we report a young woman’s case presenting with a benign phyllodes breast tumor.

Case Report

An 18-year-old Caucasian young woman was aware of a left breast lump since late 2014, and as she noticed it was growing rapidly, she came to our consultation in February 2015.

As past medical history, she had a JF enucleated in November 2010, performing follow up with clinical exploration and breast ultrasound until May 2014, with known bilateral breast stable fibroadenomas. She had a menarche onset at twelve years-old, no history of oral contraceptives intake, nullipara and nulligravida. She had no other medical conditions, previous operations or allergies. No family history of breast or ovarian cancer registered to date.

On physical examination, the patient had an augmented breast, tension of overlying skin and firmer consistency of the left breast with a palpable mass mainly located in the upper quadrant junction (Figure 1). The mass was mobile, hard, with smooth surface, well defined and deforming the breast.
Breast US showed a «bulky nodular formation of solid appearance mainly located in the upper quadrant junction of the left breast, with multiple echoes inside, peripheral vascular richness to Doppler signal and image of necrotic/liquid appearance inside. The node's dimension go beyond the diameter of the probe, and its approximate diameters are of 10.8 x 6.9 cm.

When comparing with the patient's previous study of May 2014 there is apparent stability of smaller nodules in the right and left breasts, with frank increase in volume of the nodule in the union of the upper quadrants of the left breast, meriting characterization. RB BI-RADS 2, LB BI-RADS 4 A» (Figure 2).

Core-biopsy was performed, using a 14-gauge needle, to get to a definitive diagnosis, thinking about a relapse of her giant JF, phyllodes tumor or pseudoangiomatous stromal hyperplasia considering her age.

Histology revealed «mammary gland tissue with fibrous stroma, myxoid, without cytologic atypia, with foliaceous pattern coated by ductal epithelium; can match fibroadenoma with more lax stroma or benign phyllodes tumor».

The patient underwent surgery, an upper periareolar incision through the former incision's scar was performed to excise the mass, preserving as much of the healthy breast tissue as possible. The entire integrity of the tumor’s envelope was ensured in order to guarantee safety margins (Figure 3).

Pathology described a «lumpectomy piece with 788 g and 14 x 12 x 8 cm. Bosselated external surface, integrous and entirely coated by smooth and shiny membrane. Multinodular, pearly areas at section surface, with hemorrhagic and fibro-elastic consistency. Compatible with benign phyllodes tumor. Resection with surgical safety margins» (Figure 4).
Discussion

Our young patient has had two different massive fibroepithelial tumors of the left breast in a four-year time-lapse. Breast masses in young patients are usually benign in nature but may cause considerable concern and alter breast esthetics. Despite the etiology of these massive tumors is still unknown, most hypothesis point to a hormonal basis. The hyperestrogenism hypothesis seems to be excluded since most cases in the literature have documented normal endocrine workups in these patients; nowadays the idea of an end-organ hypersensitivity of breast tissue to normal, pubertal hormone levels is widely better accepted [9,10].

Phyllodes tumor generally occurs only once and, if it occurs in high risk population, the danger of breast cancer increases significantly even before the age of 35. Very few cases of phyllodes tumor have been reported in adolescent and young women under the age of 20, most of them were classified as benign [2].

It is very important to differentiate phyllodes tumor from JF, because the latter accounts for 60% to 90% of all breast masses reported in adolescents.

Nipple discharge wasn’t present in this case, but it is usually reported in adolescents too, and it is due to infarction of the tumor. Multifocal PTs are rare; these lesions are usually unifocal as in this case [2].

In this age group, breast ultrasound is the usual imaging modality of choice due to radiation concerns. On this imaging method, FAs and PTs are seen as smooth, rounded and solid densities [10].

Most likely, the physician at this point will have made a clinical diagnosis of a FA, but a biopsy is essential for tissue confirmation, specially if it is a growing or giant mass as in this case. For solid lesions such as a fibroadenoma/phyllodes tumor, a CB is the most appropriate mean of biopsy for diagnostic purposes, can yield more tissue to be examined than fine needle aspiration, and is a way to avoid surgical biopsy [1,10].

In most cases when FA is diagnosed, a follow-up without surgery can be performed, considering its very low malignancy potential, preventing scarring and esthetic damage, but some patients choose to undergo excision of the FA for peace of mind and for body image [10].

PT are mainly differentiated from FA because of its increased stromal cellularity; however, CB specimens provide limited samples and so diagnostic dilemmas can occur between benign or borderline.
PT and cellular FA, as the degree of stromal cellularity between these entities may not be considerably different [1,12].

A revision of literature reports that CB accounts with a predictive positive value (PPV) of 52.7% in diagnosing “phyllodes tumor” or “fibroepithelial lesions with cellular stroma” on image-guided CB as they were confirmed on subsequent surgical excision; and has a PPV of 61% in excluding “phyllodes tumor” while diagnosing a “fibroepithelial lesion with cellular stroma” [1,6].

In this case, CB was accurate not excluding PT, describing it as “fibroadenoma with more lax stroma or benign phyllodes tumor”, which helped the surgeons to plan the intervention (Figure 7).

Four years before, CB was also accurate in not mentioning phyllodes tumor in the report, and diagnosing a “juvenile fibroadenoma”, confirmed after surgical enucleation of an 8 cm mass of the upper inner quadrant of the left breast (Figure 7).

**Figure 7:** (A) Hematoxylin-Eosin 20X-Juvenile fibroadenoma microscopic aspect of the surgically enucleated mass when the patient was 14 years old. (B) Hematoxylin-Eosin 10X - The same juvenile fibroadenoma. (C) Hematoxylin-Eosin 20X - Microscopic aspect of the phyllodes tumor surgically excised at 18 years of age. (D) Hematoxylin-Eosin 10X - The same phyllodes tumor.

Distinction between PT and hypercellular FA can be difficult even in surgical specimens, as these lesions are in a “grey area” and so, a 100% diagnostic accuracy of CB on fibroepithelial lesions should not be expected [1].

The standard treatment for these tumors is a breast conserving surgery with negative margins. However, in the case of positive surgical margins and once local recurrences are usually well managed with breast conserving surgery and the risk of tumor progression is low, a policy of “wait and see” attitude is accepted by several authors [5,13].

Some retrospective studies noticed that there is no significant difference in relapse after 5-year follow-up between benign phyllodes tumor surgically resected or completely removed by ultrasound guided vacuum-assisted biopsy. Randomized prospective studies are needed to confirm this observation [15].

In this case, surgical excision was undertaken through an upper periareolar incision over the scar of the previous incision, having in mind to preserve lactation ability and willing an acceptable cosmetic outcome, care was taken in order to preserve the integrity of the tumor’s envelope guaranteeing clear safety margins (no ink on tumor) and preserving as much of the healthy breast tissue as possible.

Local recurrence rate is about 14.7% for benign PT with a mean time to local recurrence of about 16 months, ranging from 8 to 32 months. Local recurrence rate is between 10 and 25% for borderline PT and between 23 and 30% for malignant PT are reported [1,5], and there is the chance of systemic spread of 22% [5]. Lung, bone and pleural metastases are observed [6]. The histologic characteristics of the recurrent tumors are similar to those of the initial tumors in 66.7% of patients, whereas the characteristics changes in 33.3%. One to two years after surgery is the recommended time for follow-up [16].

Among the benign and borderline tumors, local recurrences can be managed with further surgery, and positive surgical margins do not seem to predict a worse outcome.

When a benign or borderline tumor relapses, sarcomatous progression to malignant tumor should be taken into account, as it happens in about 4% of cases; also the risk of distant relapse is very low, <0.5% according to literature [5].

In the malignant group, there is a higher incidence of local relapse as said before, but the extent of surgery seems not to affect long-term survival [5].

Stromal overgrowth, tumor necrosis and positive surgical margins are considered negative prognostic factors, related with a significant increase of phyllodes related events. Some studies identified young age as a favorable prognostic factor [5].

Besides histology, clinical and molecular parameters are being investigated to predict a higher risk of relapse, such as immunohistochemical markers, all these markers have failed to attain any clinical validation for prognosis prediction or serving as target for therapy [5].

In this patient, clinical and US follow-up is being performed, initially with narrow surveillance until completion of two years, then normal controlled screening is intended to be done.

The patient is satisfied with esthetic result, refusing any further intervention, knowing however that she can surgically correct her slightly ptotic left breast and/or nipple-areola position.

**Conclusion**

This case report details a rare situation of a young woman having two giant non-simultaneous deforming left breast lesions; highlights the importance of CB in differentiating JF from PT and its difficulty, which determines surgical decision. A free margin excision is essential to avoid local relapse. Efforts were made to achieve an acceptable cosmetic outcome and to preserve lactation ability. As the prognosis of a benign phyllodes tumor is very good, we hope these procedures will be enough to cure this patient.

**Conflicts of interest**

The authors declared they have no competing interests.
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