Fibroadenomas of the breast: is there any association with breast cancer?

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Summary

Purpose: The experience of our Breast Unit in the diagnosis and treatment of fibroadenomas is presented in this retrospective study, focusing specifically in cancer development within these common benign tumors of young age.

Material-Methods: 310 women with histologically verified breast fibroadenomas who had surgical management in our Unit over the last 14 years were included in the study.

Results: Most of them (n: 255) presented with palpable lesions and had triple assessment preoperatively, while the remaining 55 had nonpalpable lesions and underwent needle-wire localization biopsies. Nine cases had cancer development, usually in situ, within the fibroadenomas (2.9%).

Conclusion: Coexistence of fibroadenomas and breast cancer is relatively rare, but it should not be ignored by breast surgeons, and patients should be properly informed.

Key words: Fibroadenoma; Breast cancer; Mammography; Ultrasonography; Cytology; Biopsy.

Introduction

Fibroadenomas are the most common benign tumors of the breast, the most frequent palpable masses in young women (less than 30 years old), and the most common breast abnormality following fibrocystic changes [1, 2].

Even though they are considered as tumors by most authors, some believe that they are a variation of alterations of normal development and involution (ANDI). They consist of epithelial and fibrous elements. The usual management of fibroadenomas is either follow-up or open surgical biopsy, based mainly on the size, growth rate, and the patient's age [3, 4].

The aim of this retrospective study is to present our Breast Unit policy in the management of fibroadenomas compared to the data from the recent literature. Moreover there is a specific reference to the coexistence of fibroadenomas and breast cancer.

Materials and Methods

Three hundred and ten women with histologically verified breast fibroadenomas who had surgical management in our Unit during the period January 1990 to December 2003 were included in the study.

For all cases full data about patients' age, clinical manifestations, radiologic assessment, fine needle aspiration cytology, core biopsy, surgery and histology of the surgical specimens were selected and recorded.

Statistical analysis was based on one-way variant analysis.

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Results

The patients' age was 16-60 years old (mean age: 29.5 years). Among all 310 women, 255 presented with palpable breast masses, well defined and mobile with regular borders. The remaining 55 cases had nonpalbable lesions that were revealed by screening mammograms (n: 22), and by ultrasound (n: 33) performed for various reasons (mainly for mastalgia).

All palpable cases had a triple assessment; clinical examination + radiologic tests + cytology/biopsy. Specifically, 112 had mammograms that were indicative of benign lesions (M2) in most cases (n: 105), while in seven cases the mammographic appearance was slightly suspicious (M3). Ultrasound was performed in all 255 patients and resulted as U2 (benign) in 242 of them, U3 (suspicious, but probably benign) in 11, and U4 (probably malignant) in two cases.

Following radiologic assessment, all patients with palpable masses underwent fine needle aspiration cytology (Table 1). In case of a non-diagnostic cytology or inadequate material, the aspiration was repeated. Nine out of 25 cases with a C3-C5 result had a needle core biopsy, which was B2 (showing fibroadenoma) for seven of them, and B3 (suspicious, probably benign) for two cases. The indications of the surgical biopsies for those 255 patients with palpable lumps are reported in Table 2. The mean size of the lesions was 2.4 cm (range: 1.8-7.2 cm).

All nonpalpable cases underwent an open surgical biopsy following a hook-wire localization procedure, under either ultrasonographic or stereotactic mammographic control. All lesions were successfully excised,

Table 1. – *Classification of the 255 patients with palpable fibroadenomas based on the cytology results.*

Fine needle aspiration cytoloty	No. of patients	%
C2 (benign, suggestive of fibroadenoma)	230	90
C3 (atypia)	13	5
C4 (suspicious for malignancy)	7	3
C5 (malignancy)	5	2
Total	255	100

Table 2. – *Indications for open surgical biopsy for the 255 patients with palpable fibroadenomas.*

Indications for surgical biopsy	No. of patients	%
Patient's choice	133	52
Patient's age at initial diagnosis > 35 years old	43	17
Rapid growth in size	23	9
Multiple lumps	20	8
Increased size at initial diagnosis (> 3 cm)	18	7
Patients with C3-C5 cytology, without a core biopsy	16	6
B3 core biopsy	2	1
Total	255	100

based on specimen mammograms, after one (n: 49), two (n: 5), or three (n: 1) attempts during the same surgical procedure.

The histological findings in all 310 cases were diagnostic of fibroadenomas. Moreover, in nine cases (2.9%) there was coexistence with breast cancer; four cases with in situ ductal cancer (Figure 1), one case with invasive ductal cancer, three cases with in situ lobular cancer, and one case with invasive lobular cancer. The size of the invasive tumor was very small (2-4 mm), and the tumor cells were well differentiated; therefore no further surgical treatment was required.

Among 255 patients with palpable lesions, 20 had multiple lumps (≥ 2 up to 5) in one or both breasts, and they underwent open surgical biopsy of all lesions which were fibroadenomas by histopathology. Furthermore, two out of 55 patients with nonpalpable lesions had two nodules in the same breast, and they had two separate hook-wire localization biopsies. The final histology report diagnosed fibroadenomas.

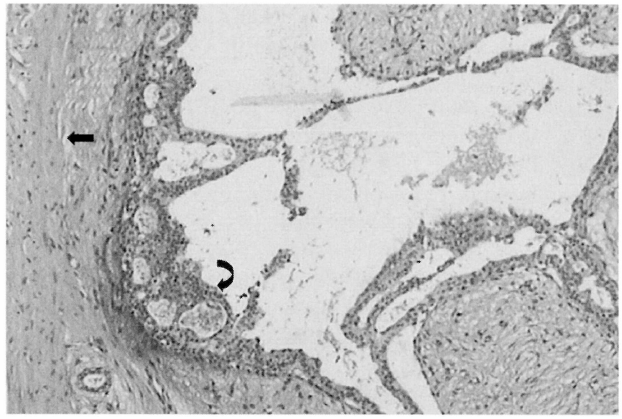

Figure 1. — Microphotograph of a fibroadenoma presenting a focus of ductal carcinoma in situ (curved arrow), which is close to the well-demarcated border that separates the fibroadenoma from the surrounding breast tissue (direct arrow).

Discussion

Fibroadenomas are benign lumps presenting in young women, usually less than 30 years old, as a result of their lobular origin and the prominent lobular proliferation in the first years after menarrche. The usual size of these lumps is 1-4 cm. During their growth phase they increase significantly in size within six to 12 months, and they remain stable or decrease later. During pregnancy they get bigger, and in postpartum they usually reduce in size [1, 3].

Mammography has limited diagnostic value for these lumps; in young breasts the increased density of the mammary gland does not usually permit the identification of breast lesions. Therefore, in our series mammograms were performed only in 112 patients (44%) who were older than 30 years. In older ages fibroadenomas have been revealed mammographically as round, well-defined masses, with similar density to the surrounding breast tissue [4]. In most postmenopausal women there is a typical benign popcorn-like calcification. Fibroadenomas can occasionally be identified on screening mammography. In our series we had 22 patients with screening-detected fibroadenomas.

Ultrasonography remains a valuable radiologic means of identification, accurate estimation of size, and follow-up of fibroadenomas. They present as round or oval well circumscribed lesions with low density, homogeneous internal echoes and a smooth wall [5]. Most of our cases had similar ultrasonographic images. Occasionally they present lobulated borders and indistinct margins. Moreover, it is essential to distinguish by breast ultrasound fibroadenomas from phyllodes tumors, which are usually benign and less common lesions; masses with circumscribed borders associated with posterior acoustic enhancement and internal cystic areas should suggest the diagnosis of phyllodes tumors [6].

Fine needle aspiration cytology of a fibroadenoma is in most cases helpful in providing enough diagnostic evidence, but false-positive and false-negative results are not rare, coexistence with cancer cannot be excluded, and there are difficulties in the differential diagnosis from phyllodes tumors [5,7,8]. The presence of hypercellular stromal fragments is a basic diagnostic feature of a phyllodes tumor [8]. All our patients with palpable masses had cytology tests of their lumps and the very good outcomes are presented in Table 1.

Core biopsy is the most valuable diagnostic test by revealing specific histologic features, and showing evidence of coexisting malignancy [9]. Even though we used core biopsies in a limited number of patients with suspicious cytology, our results were satisfactory. Moreover, specific instrumentations of core biopsy, like ultrasound-guided vacuum-assisted biopsy [10] and advanced breast

biopsy instrumentation (ABBI) [11], could achieve complete excision in all lesions up to 1.5 cm in the maximum diameter.

The management of fibroadenomas remains controversial. The usual policy for young women, when the benign nature of the lesion has been established cytologically or histopathologically, is follow-up, and in case of stable findings no surgical action is necessary [1, 3]. On the other hand some authors are more keen to offer surgery as the initial management [12]. The widely accepted indications for excision biopsy are similar to those in our series; patient's choice, large size not cosmetically accepted, rapid growth (increase in dimension > 20% for a 6-month interval) [5], suspicious findings on cytology or core biopsy [9], older patient' age, etc.

Multiple fibroadenomas are referred up to 20% [2], while in our series the respective percentage was 8.6%. Relapse of the lump postoperatively is uncommon, and is a result of either incomplete excision or multiple, not all excised, lesions in the same breast. In our series there were only two patients, 19 and 31 years old, that developed new fibroadenomas several months after their primary operation.

Coexistence of fibroadenoma and breast cancer is a rare entity, and there is not yet a well-documented etiologic association between these two conditions [9, 13, 14]. The prevalence of this entity is 0.02% in screening programs, reaching up to 6% in breast symptomatic patients [2, 14]. Most cases are non invasive cancers, usually lobular and occasionally ductal [15, 16]. Among our patients 2.9% presented cancer development within fibroadenomas, and most of them were in situ (n: 7), ductal (n: 4) and lobular (n: 3).

There is enough evidence that fibroadenomas with hyperplasia and hyperplasia with atypia present an increased relative risk for breast cancer development; up to 3.5 and 7, respectively [17]. Therefore, such patients require regular screening and careful management. Furthermore, benign lumps in women with a strong family history could more often harbor malignancy, and histologic assessment is often essential [16].

In conclusion, we should emphasize the relatively rare phenomenon of breast cancer growth within fibroadenomas; this entity should not be ignored by breast surgeons, and should be mentioned to all patients, and specially to those of an older age and with a strongly positive family history. This factor is significantly affecting patients' choice about their management; a large percentage choose excision, as in our series, instead of follow-up [15-17].

References

[1] Hindle W.H., Alonzo L.J.: "Conservative management of breast fibroadenomas". *Am. J. Obstet. Gynecol.,* 1991, *164,* 1647.

[2] Wilkinson S., Forest A.P.M.: "Fibroadenoma of the breast". *Br. J. Surg.*, 1985, *72,* 838.

[3] Cant P.J., Madden M.V., Close P.M., Learmonth G.M.: "Case for conservative management of selected fibroadenomas of the breast". *Br. J. Surg.,* 1987, *74,* 857.

[4] Brenner R.J., Sickles E.A.: "Acceptability of periodic follow-up as an alternative to biopsy for mammographically detected lesions interpreted as probably benign". *Radiology*, 1989, *171,* 645.

[5] Gordon P.B., Gagnon F.A., Lanzkowsky L.: "Solid breast masses diagnosed as fibroadenoma at fine needle aspiration biopsy: acceptable rates of growth at long-term follow-up". *Radiology*, 2003, *229*, 233.

[6] Yilmaz E., Sal S., Lebe B.: "Differentiation of phylloides tumors versus fibroadenomas". *Acta Radiol.,* 2002, *43*, 34.

[7] Rogers L.A., Lee K.R.: "Breast carcinoma simulating fibroadenoma or fibrocystic change by fine-needle aspiration". *Am. J. Clin. Pathol.*, 1992, *98*, 155.

[8] Scolyer R.A., McKenzie P.R., Achmed D., Lee C.S.: "Can phyllodes tumours of the breast be distinguished from fibroadenomas using fine needle aspiration cytology?". *Pathology,* 2001, *33,* 437.

[9] Vaideeswar P., Madiwale C., Sivaraman A.: "Carcinoma arising within fibroadenoma: a case report". *Indian J. Pathol. Microbiol.*, 2000, *43,* 87.

[10] Sperber F., Blank A., Metser U., Flusser G., Klausner J.M., Lev-Chelouche D.: "Diagnosis and treatment of breast fibroadenomas by ultrasound-guided vacuum-assisted biopsy". *Arch. Surg.,* 2003, *138,* 796.

[11] Sheth D., Wesen C.A., Schroder D., Boccaccio J.E., Lloyd L.R.: "The advanced breast biopsy instrumentation (ABBI) experience at a community hospital". *Am. Surg.,* 1999, *65,* 726.

[12] Markopoulos C., Kakisis J., Kouskos E., Kontzoglou K., Koufopoulos K., Gogas J.: "Management of nonpalpable, mammographically detectable breast lesions". *World J. Surg.,* 1999, 23, 434.

[13] Yano Y., Ueno E., Kamma H., Tsunoda H., Hara H., Yashiro T. *et al.:* "Non-invasive lobular carcinoma within a fibroadenoma, a preoperatively diagnosed case". *Breast Cancer*, 2001, *8*, 70.

[14] Yoshida Y., Takaoka M., Fukumoto M.: "Carcinoma arising in fibroadenoma: case report and review of the world literature". *J. Surg. Oncol.,* 1985, *29*, 132.

[15] Baker K.S., Monsees B.S., Diaz N.M., Destouet J.M., McDivitt R.W.: "Carcinoma within fibroadenomas: mammographic features". *Radiology,* 1990, *176,* 371.

[16] Kuijper A., Preisler-Adams S.S., Rahusen F.D., Gille J.J., van der Wall E., van Diest P.J.: "Multiple fibroadenomas harbouring carcinoma in situ in a woman with a family history of breast/ovarian cancer". *J. Clin. Pathol.,* 2002, *55,* 795.

[17] El-Wakeel H., Umpleby H.C.: "Systematic review of fibroadenoma as a risk factor for breast banker". *Breast*, 2003, *12,* 302.

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