Fibromatosis of the breast.
Report of two cases and review of the literature

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Abstract

Background: Fibromatosis is a term used to describe a group of lesions characterized by well-differentiated fibroblast proliferation with an usually benign biological behavior but with an infiltrative pattern of growth, frequently recurrent and locally invasive. It is generally localized in the retroperitoneal area, neck and extremities. The presence of this entity in breast tissue is an uncommon clinical situation, comprising ~0.2% of breast tumors and very often misdiagnosed as malignant disease or phyllodes tumor. In this rare condition, immunohistochemistry is an important diagnostic tool in anatomopathological differential diagnosis with other spindle cell tumors of the breast. The purpose of this paper is to report the experience with two cases of this rare condition.

Clinical cases: We present two cases of breast fibromatosis confirmed immunohistochemically and also by biopsy. One case had the clinical and imaging appearance of breast carcinoma with the classic irregular mass presentation and the other case was misdiagnosed as phyllodes tumor because of the size and density of the tumor and the cytology.

Conclusions: Approximately 83 cases of breast fibromatosis have been reported during the last 30 years, including one male patient. We reviewed clinicopathological features of two cases of fibromatosis of the breast treated at our institute.

Key words: fibromatosis, breast cancer

Introduction

Fibromatosis (FM) is a term proposed by Stout in 1954 to define a group of lesions characterized by fibroblast proliferation with a well-differentiated infiltrating growth pattern, with no cell malignancy but with locally invasive behavior and recurrence with surgical treatment.1

This disease has been termed low-grade fibrosarcoma, non-metastasizing fibrosarcoma, aggressive FM, desmoid tumor and specifically in the breast has been called desmoid breast tumor. Currently the term FM is generally accepted, and in the case of the breast being the primary site, it is called breast FM.2

FM comprises 0.2% of mammary tumors, which constitutes a rare tumor.3 Approximately 83 cases in the last 30 years, including a male patient, have been reported in the literature.4

There are many theories about the origin of this disease in the breast. Some authors note a history of trauma,5 previous surgery,6 breast implants,7 prior cancer,8 breast radiotherapy,8 scarring and general endocrine factors.10 Although the pathogenesis of FM generally remains uncertain, associations with this disease have already been described such as thickening of the bone cortex, exostosis, formation of bone cysts, and L5 sacralization in up to 80% of patients with FM, suggesting an abnormal regulation of connective tissue growth.11 Recently, germinal mutations were found in the APC gene and the b-catenin gene as predisposing factors to desmoid tumors.12,13

FM originates in the fibrous tissue of the breast, present in virtually the entire gland. In some cases of extensive invasion it is not possible to determine whether its origin is in the breast itself or in the pectoralis major muscle aponeurosis.8 Its growth pattern is usually infiltrative with extensions that emerge from the center of the lesion, giving it a stellate aspect.5 Despite this invasive growth into neighboring tissues, such lesions do not produce metastatic spread and their behavior is somewhat unpredictable in that some tumors grow aggressively fast and others remain static for an indefinite period of time. Spontaneous regression has even been described in some cases.14,15

The purpose of this report is to perform a literature review on the subject of breast FM and its differential diagnosis from other fusiform cell lesions of the breast and, at the same time, illustrate our experience in the management of two cases treated at our institute.
Case 1

We present the case of a 63-year-old female without a relevant history but who, on baseline mammography, is shown to have a spiculated nodule in the external upper quadrant of the right breast.

Physical examination demonstrated voluminous, pendulous, symmetrical breasts with no dominant palpable nodules or adenopathy.

Mammography reported BIRADS 5, presence of a dense spiculated nodule in the upper external quadrant of the right breast (Figure 1).

Breast ultrasound demonstrated BIRADS 5. There was a solid nodule (13 × 3 mm) of irregular margins with greater vertical diameter by posterior sonographic shadowing, localized at 10 o’clock of the right breast (Figure 2).

An ultrasound-guided core biopsy of the lesion was performed with a pathology report of a fragment of mammary tissue with recent hemorrhage. For this reason, and because of highly suspicious imaging, it was decided to perform a hookwire marking biopsy and frozen section of tissue. If results were positive for carcinoma, quadrantectomy with lymphatic mapping and sentinel lymph node dissection would be performed (Figure 3).

On February 14, 2008, hookwire marking biopsy of the right breast with intraoperative study was performed. This was inconclusive due to the presence of fibrous tissue and scarring from a previous biopsy, and the sample was referred for definitive study.

Definitive histopathology report revealed macroscopically a nodular lesion of stellate borders 1 × 1 cm with areas of fat necrosis and hemorrhage with the closest margin at 1.7 cm. Microscopically it is a lesion comprised of fusiform cells in thick bundles interlaced with oval nuclei of uniform size and scarce cytoplasm without evidence of mitosis. The stroma showed small areas comprised of dense collagen.

Immunohistochemical study was positive to vimentin, as well as being negative to AML, PS-100 and CK. Hormonal receptor study and Her-2 were triple negative.

The final diagnosis was breast FM of 1 cm at its greatest axis with free surgical margins.

Case 2

We report the case of a 61-year-old female with a history of hypertension and papillary carcinoma of the thyroid, operated and treated with $^{131}$I in 1996 and so far, with no evidence of disease. The patient presented for consultation because of self-detection of a nodule of the right breast of 5 months evolution and for which mammography and ultrasound were performed.

Figure 1. Dense, spiculated nodule in the right upper quadrant of the breast (BIRADS 5).

Figure 2. Solid nodule, 13 × 3 mm in diameter with irregular contour with posterior shadow (BIRADS 4).

Figure 3. Hookwire marking of the lesion. Lesion modified by hematoma after ultrasound-guided Trucut needle biopsy.
Physical examination revealed average size symmetrical pendulous breasts with $4 \times 4$ cm hard nodule, ill defined, in 12 o’clock position, line B, of the right breast. No adenopathies were found.

Mammography with spot compression view showed nodular dense, asymmetrical lesion of the right breast and architecture distortion with ill-defined margins and categorized as BIRADS 4 (Figure 4).

Breast ultrasound demonstrated a solid nodule with spiculated contour of $2 \times 1$ cm at the 11 o’clock position, line B of the right breast and categorized as BIRADS 4 (Figure 4).

Core biopsy revealed fusocellular neoplasm consistent with phyllodes tumor of the right breast.

The patient was scheduled for wide excision and intraoperative pathologic evaluation, which was performed on August 28, 2007. Intraoperative frozen section reported a benign fusocellular neoplasm to be classified by standard paraffin section.

Definitive histopathological report describes macroscopically a nodular, ill-defined, brown lesion ($3 \times 1.7$ cm) with irregular borders and a rubbery consistency, located 0.5 cm from the deep margin and >1 cm from the rest of the margins. Microscopic evaluation showed a lesion consisting of fusiform cells arranged in thick intertwined bundles with uniform-sized oval nuclei and scant cytoplasm with dense stromal collagen. The lesion infiltrated the adjacent adipose tissue and surrounded mammary ductal structures but did not show alterations (Figure 5).

Immunohistochemical studies were strongly positive to vimentin (Figure 6) and negative to cytokeratin, AML and S-100. Estrogen and progesterone hormone receptors and Her-2 assessment were triple negative.

The final diagnosis was breast FM (3 cm at its greatest axis) with tumor-free surgical margins.

**Discussion**

For practical purposes in breast pathology, some authors include FM in the chapter of “fusiform cell lesions of the breast,” which describes all non-neoplastic and neoplastic lesions with a predominance of fusiform cells and for this reason it is necessary to make the differential diagnosis and thus avoid excessive or insufficient treatments. Among the most frequently mentioned diseases to differentiate are fibrosarcomas, diabetic mastopathy, and leiomyomas, among others.

The presence of fusiform cells in a breast lesion may be seen in any of these pathologies and, therefore, clinical findings and imaging studies, as well as cytological and histological studies clarify the diagnosis in the great majority of the cases. Performing a careful examination of the accompanying epithelial element and with the support of immunohistochemical studies, all these lesions could be diagnosed by means of a core biopsy. Cytology using fine needle aspiration is considered an insufficient method for reaching a diagnosis of FM, as well as of other pure fusiform cell tumors.
Currently, we are attempting to include many of these lesions that are positive to immunohistochemistry, vimentin and CD34 and classified as benign breast stromal tumors.

At present, immunohistochemistry is a fundamental and required instrument for definitive diagnosis of FM. These lesions have an initial cellular growth phase and a less cellular with mature fibroblasts and abundant collagen late phase, where the central portion of the tumor is usually hypocellular with greater hypercellularity towards the periphery. On electron microscopy these lesions are composed of fibroblasts and myofibroblasts in variable proportions, being positive to vimentin and rarely to desmin in immunohistochemical studies.

FM behaves as fibromatosis in other locations, for which they are locally invasive and refractory to surgery if not completely excised with wide margins. A bilateral synchronous presentation associated with Gardner syndrome has been described as well as a metachromic form. Due to its association with intestinal polyposis syndrome, a colonoscopy is recommended in these cases. FM may clinically and immunologically mimic breast cancer, especially scirrous carcinoma, for which it has sometimes been treated erroneously. Three cases of mastectomies have been reported with an initial diagnosis of carcinoma in patients with FM. It may also be confused with benign lesions such as fibroadenoma or phyllodes tumor.

FM presents as a mammography finding or as a palpable hard, solid and irregular nodule. During its evolution the tumor may grow, producing skin tethering and nipple retraction, as with breast carcinoma, producing invasion and/or fixation to the pectoral muscle and to the chest wall as well as the rectus abdominis muscle aponeurosis. Despite its locally aggressive and recurrent behavior, no distant metastasis has been found. When these nodules appear, FM should be suspected.

Povoski et al. reported the association of FM with breast cancer without establishing if the relationship is with the neoplasm itself or as a

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RT, radiation therapy.
result of its treatment\(^4,34\) (surgery and radiation). Mammography, as well as ultrasound, could report solid spiculated masses with irregular contours with the appearance of carcinoma.\(^5,35\)

In nuclear magnetic resonance (NMR), some Japanese authors report that the imaging of fibromatosis is not similar to that of cancer, for which it may be an instrument for the differential diagnosis. The study is performed in axial projection with contrast and fat suppression. In T1-weighted images, a lesion with ill-defined margins is observed with heterogeneous appearance. In the dynamic phase after injection of contrast there is a gradual uptake of contrast medium.\(^36\) However, other authors report similar images to that of cancer in cases of FM.\(^37\)

Malignant transformation of FM has been reported by Soule et al. in a case where recurrence, after having been treated with surgery and radiotherapy, resulted in FM.\(^38\)

Therapy in FM is similar to extramammary FM. Treatment is summarized in a wide excision with tumor-free margins.\(^8\) The techniques described include lumpectomies, local wide excision, quadrantectomies\(^13\) up to simple mastectomy even extended to the thoracic wall\(^7\) (with thoracic wall resection) in voluminous tumors or those that infiltrate the skin or the chest wall where the surgery should be more radical in order to achieve tumor-free margins. Axillary dissection is not necessary in these cases unless there is direct tumor invasion in this area. Some authors recommend histopathological control of all surgical margins,\(^26\) including orientation of the surgical specimen and intraoperative study;\(^15\) however, Gump et al. reported their difficulty in evaluating the margins on FM intraoperatively and, similarly, have followed patients with close and positive margins for many years with no evidence of relapse.\(^15\)

Trucut biopsy and observation of the lesion may be an acceptable behavior in tumors of stable behavior where their stability is demonstrated with evolving studies.\(^39\)

Other modalities of treatment have been popularized, such as adjuvant radiotherapy and hormone therapy with anti-estrogens. Given the low frequency of the disease, the results appear to be controversial. However, many authors agree that in the presence of recurrent disease or lesions whose resections leave positive or close margins, radiotherapy is an acceptable action.\(^7,25,26,29,40\)

Recurrences have been described in a range from 4 months to 20 years after surgery, and most authors report that it is later than in breast cancer, so in case of mastectomy one should wait at least 3 years in planning breast reconstruction.\(^41\) The presence of close or positive margins is a factor that increases the risk of recurrence.\(^20,41\)

The experience with this disease is limited and the largest numbers of cases have been reported by Wargotz et al. with 28 patients.\(^20\) These authors reported having achieved adequate local control in 75% of cases with wide excision. No deaths were reported from the disease. Gump et al. published a series of 13 cases of which three cases were recurrent.\(^15\) In other publications, the number of cases is too limited with an average of one or two cases.\(^42-44\)

In conclusion, FM is a benign neoplasm of fibrous breast tissue, which can clinically and by imaging studies simulate breast cancer or phyllodes tumor, among other lesions. Its behavior is locally aggressive and should therefore be treated with oncological criteria. Trucut biopsy of the lesion and the application of immuno-histochemical techniques lead to preoperative diagnosis in most cases. The use of radiotherapy and hormone therapy has not yet been standardized. In our experience, these lesions were clinically confused with carcinoma and phyllodes tumor; however, diagnosis of a benign tumor in intraoperative studies made it possible to avoid excessive surgery in these cases.

References


