Myofibroblastoma of the Breast: Diagnostic Challenges of a Rare Benign Tumor

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Abstract Breast myofibroblastomas (MFBs) are rare benign tumors that have recently been recognized as a distinct entity. They are more common in men and often coexist with gynecomastia. Fine needle aspiration cytology or core biopsy should always be performed for triple assessment; however, due to the multiple variants of the tumor, final diagnosis can be safely accomplished only postoperatively with the aid of immunohistochemistry. The main histological characteristic that differentiates MFBs from the majority of malignant mesenchymal breast lesions is the presence of spindle cells in a collagenous background. Low mitotic activity and vimentin and CD34 positivity have been reported as well. Surgical excision retains a pivotal diagnostic and curative role. Local resection is sufficient, but mastectomy can also be advocated either in cases of male patients with coexisting gynecomastia or in females with large tumors. Into this retrospective survey, three cases of breast MFB were consecutively enrolled. Two patients were postmenopausal females and one was male. Relevant literature is briefly reviewed. Clinical features, histogenesis, morphological, and immunochemical findings are discussed, while the role of the current diagnostic and therapeutic management of this uncommon neoplasm is emphasized.

Keywords Myofibroblastoma · Breast lesions · Benign spindle stromal tumors

Introduction

Breast myofibroblastomas (MFBs) are rare benign tumors that have recently been recognized as a distinct entity. They are more common in men and often coexist with gynecomastia. Nevertheless, when these tumors are present in women, establishing a diagnosis may be quite challenging [1]. The absence of malignant features on clinical examination and subsequent imaging is typical. Fine needle aspiration cytology (FNAC) or core biopsy should always be performed for triple assessment; however, due to the multiple variants of the tumor, final diagnosis can be safely accomplished only postoperatively with the aid of immunohistochemistry [2]. The main histological characteristic that differentiates MFBs from the majority of malignant mesenchymal breast lesions is the presence of spindle cells in a collagenous background. Low mitotic activity and vimentin and CD34 positivity have been reported as well [3]. The aim of this investigation was to analyze all cases of breast MFB presented in our institution. Relevant literature is briefly reviewed. Clinical features, histogenesis, morphological, and immunochemical findings are discussed, while the role of current diagnostic and therapeutic management of this uncommon neoplasm is emphasized.

Methods and Results

The records of the patients registered in the Breast Clinic of the 2nd Department of Surgery of Aretaieion University Hospital from 01 January 1999 to 31 December 2009 were subjected to meticulous examination. Into this retrospective survey, three cases of breast MFB were consecutively enrolled

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(Table 1). Two patients were postmenopausal females and one was male. In all patients, the tumor presented as a smooth, mobile, nontender palpable mass (Fig. 1). In the two cases, the lesion was measuring less than 4 cm, while in the case of the male patient, the mass measuring 70 mm had been palpable and slowly growing over a period of 6 months. Gynecomastia has not been reported. Over the last weeks, inflammatory signs appeared over the tumor area, and the patient decided to seek medical affection. No patient appeared with enlarged axillary lymph nodes on clinical examination. Ultrasonography (U/S) result showed a solid, homogeneously hypoechoic, and well-defined lump. Subsequent mammography revealed a well circumscribed mass. FNA was not diagnostic in the case of the male patient; however, in the other two cases, it was suggestive of a nonmalignant mesenchymal disorder. Taking into consideration the benign findings on imaging, lumpectomy was decided for the male and for the 53-year-old female patient with the negative FNA. As for the third case, although the preoperative diagnosis was indicative of a benign neoplasm, mastectomy was performed due to the tumor's dimensions.

Macroscopically, all lesions were white to gray on sections, round to lobulated, and deprived of true capsule. Neither hemorrhage nor necrosis was present. Microscopically, the predominant cellular type was the spindle cell; however, in the second

Table 1 Clinical, cytological, and histological characteristics of MFB patients

	Case 1	Case 2	Case 3
Age/sex	78/M	53/F	75/F
Size (mm)	30	16	70
Clinical presentation	Palpable mass without gynecomastia	Palpable mass	Palpable mass over 6 months
FNA	–	Mesenchymatous tumor	Mesenchymatous tumor
Operation	Lumpectomy	Lumpectomy	Mastectomy
Cell type	Spindle	Spindle/adipose/epithelial	Spindle
Atypia	–	–	+
Mitosis	0–1	0–1	0–1
Matrix	Collagenous	Myxoid	Collagenous
Vimentin	+++	+++	+++
CD34	++	++	+++
Desmin	+	+++	–
ER	+	+++	+
PR	+++	–	–
AR	+	–	–
SMA	–	–	+
S-100	–	–	–
Ki-67	<10 %	<10 %	<10 %

MFB myofibroblastoma, F female, M male, FNA fine needle aspiration, ER estrogen receptors, PR progesterone receptors, AR androgen receptors, SMA smooth muscle actin

Fig. 1 U/S depiction of breast myofibroblastoma

case, adipose tissue and epithelial cells were also detected. The bipolar spindle cells that characterized all tumors had elongated nuclei and were arranged in fascicles and surrounded by myxoid to collagenous matrix (Fig. 2). Cellular atypia was found only in one case, and mitotic activity was infrequent (0–1 HPF). Immunohistochemistry established the diagnosis in each case. Vimentin, CD34, and estrogen receptors (ERs) were consistently positive, while the expression of desmin, progesterone receptors (PRs), and androgen receptors (ARs), and smooth muscle actin (SMA) varied (Figs. 3 and 4). S-100 protein was negative. Similarly, Ki-67 was less than 10 %, indicating minimal proliferation. Median follow-up time was 5 years. Local recurrence was not apparent. The male patient died 8 years after the surgical procedure from acute myocardial infarction, and the two female patients remained alive and disease-free.

Discussion

Mammary MFB belongs to the family of benign spindle stromal tumors of the breast, which includes various neoplastic

Fig. 2 Histological section of the breast myofibroblastoma showing bundles of elongated cells with spindled nuclei (hematoxylin–eosin, $\times 100$)

Fig. 3 Histological section of the breast myofibroblastoma showing extensive and intense cellular immunoreaction to vimentin (immunostain, $\times 100$)

lesions, all originating from a precursor cell of the mammary gland [4]. This type of tumor was initially recognized in 1981. Six years later, Wargotz et al. elucidated 16 cases of a distinctive benign mesenchymal tumor named MFB [5]. So far, single case reports or small case series have been reported in the literature.

MFB predominates in adult males. The age at presentation ranges from 40 to 87 years [6]. The size of the tumor does not usually exceed 4 cm, with the exception of a case of a giant MFB measuring 10 cm. The etiology of MFB remains controversial. Several lesions have been identified in patients presenting with gynecomastia, while an etiologic association with sex steroid hormones has been advocated by many authors, as nuclear estrogen, progesterone and androgen receptors were apparent in the majority of the cases [4, 6]. Taking into account the role of myofibroblast in collagen synthesis and cellular contraction after injury, MFBs would be expected to present at postinjury or postsurgical sites; nevertheless, only a few such cases have been described.

Histologically, there is a great variety of cellular composition, extracellular matrix, and growth pattern reflecting the origin of the tumor from a pluripotential mesenchymal cell. Magro has described a variety of histologic patterns in breast

Fig. 4 Histological section of the breast myofibroblastoma showing positive cellular immunoreaction to desmin (immunostain, $\times 100$)

myofibroblastoma: (1) the cellular, (2) the infiltrating, (3) the collagenized/fibrous, (4) the lipomatous, (5) the myxoid, (6) the epithelioid, and (7) the deciduoid-like variants. Typically, spindle cells are arranged in short haphazardly intersecting fascicles or clusters, interrupted by collagen bundles [7]. The lack of ducts and lobules in the lesions, and the minimal vascular component are characteristics [4]. Myofibroblasts, fibroblasts, adipocytes, smooth muscle cells, chondrocytes, and osteoblasts can all be encountered in MFBs, expressing their common origin from a precursor stromal cell. Essential elements for diagnosis are the presence of thick hyalinized collagen bundles and low mitotic activity in addition to the lack of myoepithelial component and necrosis [8].

Immunohistochemistry confirms the diagnosis, adds valuable information in ambiguous cases, and excludes malignancy. Vimentin and CD34 are consistently positive, while the expression of desmin, SMA, bcl-2, and CD99 varies [9]. Cytokeratins, c-Kit, and S-100 protein are constantly negative [4]. Estrogen and progesterone receptors are usually expressed. Differential diagnosis of MFB can be complex, especially when certain subtypes with morphological variations are examined. Sarcoma, invasive lobular carcinoma, spindle cell carcinoma, fibromatosis of the breast, leiomyoma, or myxoid tumors should all be considered and excluded based on histology and immunohistochemistry.

Clinically, MFB is an asymptomatic, solitary, well-circumscribed, firm, and mobile lump that grows slowly. Sometimes, it presents as an incidental finding in case of gynecomastia [5]. Enlarged axillary lymph nodes or skin and nipple changes are not documented. U/S depicts a solid, homogeneously hypoechoic, isoechoic, or hyperechoic lesion. When the tumor appears hypoechoic, it might mimic fibroadenoma. However, there have been described hyperechoic lesions with posterior acoustic shadow. Mammography usually reveals a well circumscribed, dense mass without calcifications or halo sign. The tumor may also appear with ill-defined margins with coarse calcifications. It may be round, oval, or lobular in shape or it may be mammographically occult [7, 10]. Differential diagnosis includes fibroadenoma and phylloides tumor; round pattern gynecomastia; neurofibroma; lymphangioma; hematoma, abscess, carcinoma, and sarcoma. Magnetic resonance imaging demonstrates a well-circumscribed mass with homogeneous enhancement with internal septations. Nevertheless, it was not implemented, as U/S and mammogram results are suggestive of a benign lesion [11]. FNAC is helpful in establishing the preoperative diagnosis, provided it is evaluated in combination with clinical and radiological information. Core biopsy is always a safer option as more information can be obtained, although the pleomorphism of MFBs can lead to diagnostic pitfalls [12].

Surgical excision retains a pivotal diagnostic and curative role. Local resection is sufficient, but mastectomy can also be

advocated either in cases of male patients with coexisting gynecomastia or in females with large tumors. Macroscopically, MFB is a well-circumscribed, sometimes lobulated, smooth or firm, nonencapsulated, pale white to grayish mass with pushing borders [13]. Infiltrating margins have been reported in only one patient; nevertheless, a pseudocapsule of compressed fibrous tissue is typical [14]. Prognosis of MFB is excellent, and local recurrence has never been implied.

Conflict of interest None

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