Annals of Medical and Clinical Oncology
Ubbaonu CD, et al. Ann med clin Oncol 6: 156.
www.doi.org/10.29011/2833-3497.000156
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Case Report

Myofibroblastoma of the Male Breast: a Typical Case Report and Narrative Review

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Citation: Anna S, Dimitrios V, Federico F, Vinicio DF, Fronis C, et al. (2023) Myofibroblastoma of the Male Breast: a Typical Case Report and Narrative Review. Ann med clin Oncol 5: 156. DOI: https://doi.org/10.29011/2833-3497.000156

Received Date: 15 September, 2023; **Accepted Date:** 22 September, 2023; **Published Date:** 25 September, 2023

Abstract

Myofibroblastoma (MFB) is a rare stromal benign tumor that arises from the breast tissue, composed by fibroblasts, myofibroblasts and adipocytes. MFB typically presents as a solitary, painless mass in the breast, predominates in 60-80 years-old adult males and is rarer in postmenopausal women. It could be diagnosed by a combination of imaging and pathological tests, even if its imaging features are nonspecific, often leading to misdiagnosis. Biopsy is always needed for definitive diagnosis. Wide local excision, with no need of sentinel lymph node biopsy, is curative since local recurrence is extremely low and has been reported to be less than 1.5%. We report herein the case of MFB in a 61-year old male presenting with a nodule on the left breast and review the literature focusing on differential diagnosis.

Keywords: Myofibroblastoma; Breast cancer; Male breast; MFB.

Introduction

Breats MFB, or myogenic stromal (mesenchymal) tumor, of the breast is a rare benign tumor derived from mammary stromal fibro-myofibroblasts, first described by Wargotz et al. in 1987 as a distinctive stromal tumor, nodular and well demarcated, formed by uniform, slender, bipolar spindle cells [1]. It is composed of a variety of cells including fibroblasts, myofibroblasts (spindle-shaped cells that play a role in the formation of connective tissue) and adipocytes. It is more common in male patients of older age [2,3] and typically presents as a solitary, painless, movable, palpable mass in the breast, usually not exceeding 3 cm of diameter, even if it is described from 2 mm to 18 cm [2,4,5]. It is usually diagnosed by a combination of imaging and pathological tests, such as mammography, ultrasound, and biopsy, and diagnosis requires a correlation between clinical and instrumental findings.

Case presentation

We report a case of a 61-year-old male, without family history of breast cancer family history of breast cancer, presenting with a palpable mass on the left breast, diagnosed and treated in the department of Propaedeutic surgery of the Aristotle University of Thessaloniki. Written informed consent was obtained from the patient for the publication of any potentially identifiable images or data included in this report. The patient was subjected to a CT scan after noticing dizziness and fainting after starting a therapy with alpha-blockers for prostatic hyperplasia. In CT scan was incidentally detected a dense, well-circumscribed, rounded mass,

without halo sign, in the left breast.

He presented with a nodule on the upper outer quadrant measuring 2 × 1,5 cm, well circumscribed, and freely movable. He had no skin or nipple retraction, and no palpable axillary lymph nodes.

Mammograhy (CC, MLO, Figure 1) showed a radiopaque, hyperdense mass in the upper-outer quadrant of the left breast, with a maximum diameter of 2,5 cm, without evidence of pathologic microcalcifications (BI-RADS 4c).

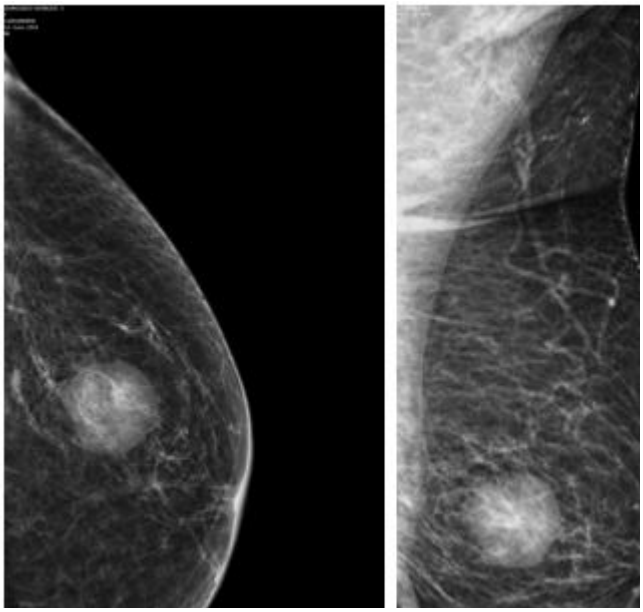

Figure 1: Mammography (CC, MLO) showing a radiopaque, hyperdense mass in the upper-outer quadrant of the left breast.

Ultrasound (US) revealed a hypoechoic mass with diameter of 2,2 x 1,53 cm, located at 2 o'clock position in the left breast, 2 cm far from the nipple, with unspecified boundaries and hypervascularized at color-doppler. No pathological findings were found in the right breast or in the axillary lymphnodes.

According to the US results a core biopsy was performed, and showed extensive occupation of small, ovoid, monomorphic neoplastic cells, without cellular or nuclear atypia and arranged individually or in small bundles, CD34+, ER+, demin+, with granular cytoplasmic staining in β-catenin, but negative in pancreatin and in STAT-6, compatible with MFB of the breast.

Considering the radiological examination and the benign pathological findings a local excision was performed. The mass was well defined, demarcated and encapsuated, did not infiltrate the mammary gland, the skin or the pectoral muscle.

The histopathologic exam revealed macroscopically a 2,5 cm well-circumscribed, solid capsulated, pale white to grey round mass with nodulated surface (Figure 2).

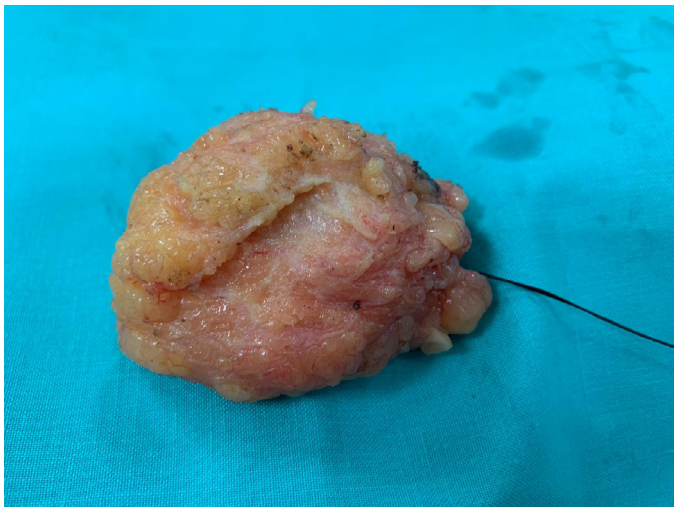

Figure 2: Surgical specimen.

Microscopically, the mass consistsed on small, ovoid, monomorphic spindle cells arranged in haphazardly intersecting fascicles or clusters, thick hyalinized collagen bundles and low mitotic activity with a lack of cellular or nuclear atypia, myoepithelial component or necrosis, and arranged individually or in small bundles (Figure 3A, 3B).

Immunohistochemistry the lesion showed expression of CD34 (expressed on haematopoietic cells, or in mesenchymal stem cells), actin and desmin (patched). Estrogen, progesteron and androgen receptors were positive and pancreatin and STAT-6 were negative (Figure 3C and 3F).

After 12 months, the patient shows no signs of recurrence.

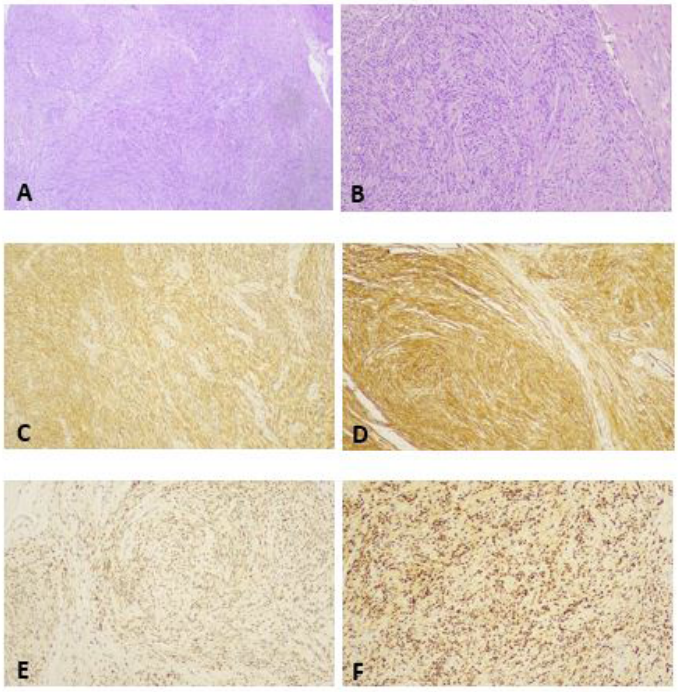

Figure 3: Histological features; 2A: H&E x 04. 2B: H&E x 10. 2C: BCL 2 staining X 10. 2D: CD34 staining X 10. 2E: ER staining X 10. 2F: PR staining X 10.

Narrative review

Epidemiology

MFB is a rare neoplasm, belonging to the family of benign spindle stromal tumours of the breast, and the number of cases reported in the medical literature is relatively small. It was first described by Wargotz et al in 1987, who reported 16 cases of well demarcated male breast nodules, formed by "uniform, slender, bipolar spindle cells haphazardly arranged in fascicular clusters separated by broad bands of hyalinized collagen" [1].

It is generally considered to be more common in men than in women, in which usually occurs in middle age, while in men it is more common in older age groups. It represents less than 1% of breast tumours [2].

It is reported also associated with treatment for prostate hyperplasia/tumor [6], gynaecomastia [7] and male-to-female transgender patients treated with feminilizing hormones [8], and in some cases could be associated with invasive breast carcinoma [6] or radiation therapy [9].

Less commonly, MFB can originate from extra-mammary sites (extramammary MFB), mainly female genital tract and soft tissues along the milk line (inguinal region, axilla, trunk, chest wall), in rare cases intra-abdominal, retroperitoneal or localized in the extremities [10]. In rare cases it was observed multiple and bilateral MFBs [11,12].

Clinical and radiological findings

Myofibroblastoma of the breast typically presents as a solitary, painless breast mass. On physical examination, the mass may feel rubbery or firm to the touch and may be mobile or fixed. Other symptoms such as nipple discharge, skin changes, or lymph node enlargement are not usually associated with myofibroblastoma [13].

The mass is usually well-circumscribed, round or oval-shaped mass with smooth margins, and for this reason imaging is often non-specific and differential diagnosis is challenging [2,14].

On mammography usually it appear as a homogeneous, circumscribed mass with high to intermediate density (hyperdense or isodense), without microcalcifications [15,16].

On ultrasound MFB usually has generally a hypoechoic appearance and can be visualized as a solid and well-circubscribed mass, or it may contain areas of cystic degeneration [15], even if some cases reported hyperechoic MFB [17].

Magnetic resonance imaging (MRI) can also be used to evaluate myofibroblastoma, and it typically shows a well-circumscribed mass with low to intermediate signal intensity (isointense or hypointense) on T1-weighted images and high signal intensity (hyperintense) on T2-weighted images [16,18], even if some Authors reported cases of MFB with hypointense and hyperintense central core surrounded by a hypointense capsule in T2-weighted images [19].

Pathological findings

On gross examination, MFB appear as solid, well-circumscribed, encapsulated lump, with gray nodular surface [2, 10]. In a minority of cases could be multilobulated [20].

On microscopic examination, in most cases the tumor is composed of spindle-shaped cells with elongated nuclei, called myofibroblasts, disposed randomly and embedded in a fibrous or collagenous stroma, with variable amount of fat tissue and without a true capsule. When the fat tissue is predominant (> 75%), it is called lipomatous MFB [3,21] and for this variant differential diagnosis with spindle cell lipoma could be challenging [3]. In some cases, histology of MFB could show tortouous, "staghorn-like" vessels surrounded by perivascular hyalinization, and could resemble a solitary fibrous tumor [22,24]. Even this cases, differential diagnosis could be difficult, because solitary fibrous tumor show similar immunohistochemical characteristics (in particular, CD34+, vimentin+ and SMA+) [25].

Normally myofibroblasts show small nucleoli, low mitotic activity (without atypical mitoses or necrosis) and sporadic cytologic atypia [10]. However, some cases may show atypical or pleomorphic features (such as cartilaginous or osseous differentiation [26].

Another variants are leiomyomatous MFB, in which cells with smooth muscle cell differentiation with cigar-shaped nuclei (myoid) are present and H-caldesmon staining can be positive [27,28]; and myxoid MFB, in which there are diffuse myxoid changes [14,29,30]. This latter goes in differential diagnosis with other myxoid neoplasms, such as like low grade fibromxyoid sarcoma [31].

Moreover, some other variants have been described, such as cellular MFB [32], deciduoid [33], epithelioid [34], atypical [35], infiltrating [36] and with hemangiopericytoma-like pattern [22], so careful examination is necessary to differentiate them from other spindle cell tumors, such as spindle cell carcinoma or sarcoma.

Immunohistochemical staining can help confirm the diagnosis of MFB. MFB typically shows positive staining for vimentin, desmin, SMA, hormonal receptors (ER and PR), BCL2, CD99, CD10 and often shows a characteristic pattern of CD34 staining, with strong positivity in the fibrous stroma surrounding the myofibroblasts. In MFB with smooth muscle differentiation, could be found positivity for H-caldesmon [28], [27], while it is usually negative for HER2/neu, Cytokeratins, S100, p63 CD117, and Rb [2,10].

Treatment and outcomes

Treatment for MFB usually involves surgical removal of the tumor, and the prognosis is generally excellent with no recurrence after complete excision.

Discussion

It is important to differentiate MFB from other stromal lesions of the breast, fibroadenoma, phyllodes tumour, round pattern gynecomastia, spindle cell carcinoma and breast sarcoma, to avoid performing unnecessarily extensive procedures.

On clinical exam, MFB could be easily confused with fibroadenoma or phyllodes tumour in female patients or round pattern gynecomastia in men, in its classic form (rubbery, mobile, and painless mass). In its less common presentations could be confused with breast tumors.

The radiological presentation of myofibroblastoma can be similar to other benign and malignant breast tumors. Ultrasound appearance can be often similar to fibroadenomas, phyllodes tumor or gynecomastia [15], because of the round and well-circumscribed appearance, without signs of retraction or acoustic shadowing. Typical ultrasound appearance could be a mix of fibroadenoma and phylloides tumor, since there is a hypoechoic heterogeneous mass (like phylloides tumor), but well-circumscribed and hypovascular (like fibroadenomas).

Mammographic images are similar to angiolipomas, fat necrosis or fibroadenomas [37], because of circumscribed margins and the absence of microcalcifications. Also MRI findings are not distinctive and variable, since T1 hypointensity and T2 hyperintensity could be similar to spindle cell carcinoma or breast sarcoma [38,39].

Distinctive signs of MFB are often hard to find, and often a fine needle biopsy is usually necessary to confirm the diagnosis and differentiate from other breast masses.

Fortunately histopathologic specimen differs from the most common benign and malign breast masses (fibroadenoma, ductal and lobular carcinoma), even if the presence of spindle-shaped cells embedded in a fibrous or collagenous stroma could be similar to other stromal benign or malign tumors (like breast sarcoma or spindle cell carcinoma) [40,41], so immunochemistry is fundamental. In the majority of cases, the association of positive staining for vimentin, desmin, SMA, CD34 and ER and negativity of p63 and CK could be diriment (Table 1).

	MFB	Fibroadenoma	Phylloides tumor	Spindle cell carcinoma	Breast Sarcoma
Ultrasound	Hypoechoic, solid, heterogeneous, well-circubscribed, hypovascular	Hypoechoic, homogeneous, oval, circubscribed, horizontal axis, smooth/ lobulated border, hypovascular [42]	Hypoechoic, heterogeneous, irregular shape, irregular / microlobulated / indistinct margins, hypervascular [43]	Heterogeneous, round, internal vascularity, indistinct margins, posterior acoustic shadowing [38]	Hypoechoic, oval or irregular, indistinct or microlobulated, internal vascularity, posterior acoustic shadowing [39,44]
Mammography	Homogeneous, circumscribed, hyperdense or isodense, no calcifications or distortion	Oval, circumscribed, hyper- or hysodense [43]	Oval/irregular, often irregular/ lobulated margins, hyperdense [43]	Round/lobulated, spiculations/ architectural distortions, occasional pleomorphic or linear calcifications [45]	Oval/lobular/ round, indistinct or microlobulated margins, architectural distortion, hyperdense or isodense, occasional calcifications [39,44]
Breast MRI	Circumscribed mass with, isointense or hypointense on T1, hyperintense on T2	Oval, homogeneously enhanced [43]	Irregular, heterogeneously enhanced [43]	Irregular, spiculated, hypointense in T1, hyperintense in T2, variable enhancement [38]	Irregular, spiculated, hypointense or mixed in T1, hyperintense in T2, variable enhancement [39]
Histology	Myofibroblasts disposed randomly with fibrous or collagenous stroma and variable amount of fat tissue	Homogeneous nodular proliferation of fibroblasts, stromal proliferation around glands, without atypia [38]	Heterogeneous fibroepithelial architecture, stromal hypercellularity with fronded architecture, variable nuclear atypia [46]	80% spidle cell with fascicular, storiform, or haphazard growth pattern, infltrative border, cytological atypia [47]	Widely infiltrative borders, spindled cells, variable pattern, necrosis [40]
IHC	Vimentin+, desmin+, SMA+, ER+, CD34+, PR±, BCL2±, CD99±, CD10± H-caldesmon±, Her2-, S100-, p63-, CD117-, Rb-, CK-		CK-, p63-, CD34+, CD117+ (high grade), Bcl2+ [46]	CK+, p63+, ER-, PR-, Her2- [47]	Vimentin+, S100+, CD34+, CK-, high mitotic index, ER-, PR-, Her2- [40]

Table 1: Differentiate MFB from other stromal lesions of the breast.

Conclusions

Nonetheless, MFB of the male breast is still a relatively uncommon diagnosis, and further research is important to determine the correct diagnosis, to better understand its incidence, prevalence and treatment and anticipate the identification and differentiation with other breast masses.

Disclosure

Author Contributions

All Authors contributed equally to the development of this paper.

Funding

This research received no external funding.

Informed Consent Statement

Written informed consent has been obtained from the patient to publish this paper.

Conflicts of Interest: None.

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