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Mammary Myofibroblastoma: Case Report and Review of the Literature

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Abstract

Myofibroblastoma (MFB) is a relatively rare breast tumor that belongs to the family of the "benign stromal tumor of the breast." The differential diagnosis of MFB includes several reactive, benign, or even malignant entities. A definitive diagnosis of myofibroblastoma can have histomorphological challenges, requiring ancillary studies. There have been <100 published case reports of mammary MFB reported to date after being first described as a distinct entity in 1987. The clinical significance of this entity lies primarily in its recognition as a distinctive benign neoplasm. We present a case of MFB and review the literature to expand upon the current literature.

Introduction:

Mammary myofibroblastoma (MFB) is a rare benign tumor of myofibroblastic differentiation described in different sites such as soft tissues, skin, lymph nodes, and breasts.[1] The prevalence is unknown but probably accounts for <1% of all breast neoplasms with an age distribution ranging from 25 to 87.[2] The tumor has a mesenchymal origin and is characterized by the proliferation of fusiform cells surrounded by collagen derived from fibroblasts. They do not metastasize and have a low rate of recurrence.[3] At clinical examination, it generally presents as a unilateral, solitary, firm, mobile, and painless breast mass with slow growth.[4] MFB can arise in extra-mammary sites along the milk line and has been reported in the literature in different locations, including the axilla, tonsil, lung, rectum, meninges, prostate, parotid gland, and tongue.[5] Malignant transformation has not been reported yet. There is only one case in the literature of recurrence of MFB at the previous excisional site.[5] This type of tumor causes differential diagnostic problems by mammography and ultrasonography, as it appears in several different variations and, for example, can be confused with hamartoma or fibroadenoma.[6] There has been no report in the literature regarding diagnostic treatment modalities, but breast ultra sound (US) sonography, mammography, and US-core needle biopsy are strongly recommended to obtain a diagnosis before surgery.[5]

Case Presentation:

A 59-year-old woman presented to the clinic with a 4 cm painless breast mass. She had no history of malignancy or significant medical conditions. However, her mother died of breast cancer at the age of 63. The mass was detected on routine mammography screening as a well-defined soft-tissue density in the upper outer quadrant of the left breast without any evidence of microcalcification. Fine needle aspiration cytology of the mass was performed, but the results were inconclusive, and a decision was made to remove the mass with adequate safe surgical margins surgically.

The excised 4 cm mass grossly showed a glistening lobulated adipose tissue with intervening white tan fibrous-like areas, with no evidence of hemorrhage or necrosis. Microscopic examination revealed spindle cells arranged in fascicles, with foci of nuclear palisading traversed by broad fibrocollagenous areas and multiple thick-walled blood vessels (Figure 1A). Focal infiltration into the fatty tissue was noted. Although the spindle cells of the tumor showed focal nuclear enlargement, only rare mitotic activity was reported (<1/40 HPF) with no evidence of necrosis (Figure 1B). The histomorphologic diagnosis was a spindle-cell tumor with a benign appearance. Immunohistochemistry (IHC) studies were essential to classify the tumor further and rule out possible malignancy. The tumor cells were positive for

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vimentin, CD34 (Figure 1C), estrogen (Figure 1D), and SMA (smooth muscle actin) while negative for cytokeratin Cam 5.1, S100, desmin (only focally positive), h-caldesmon and myogenin. Ki-67 nuclear staining was <2% indicating low proliferation of the tumor cells. The immunoprofile and the histologic findings were diagnostic of benign mammary myofibroblastoma. All surgical margins were free of tumors. The patient was followed up for four years with no evidence of recurrence, after which she was lost to follow-up.

Discussion:

Myofibroblastoma was first described in 1981 and was named by Wargotz et al. in 1987, using a series of 16 cases in which 11 patients were men, and the average age was 63 years.[7] It is typically a bland-looking spindle cell tumor exhibiting morphological, immunohistochemical, and ultrastructural features of fibroblasts and myofibroblasts differentiation.[8] MFB can arise in extra-mammary sites along the milk line and has been reported in the literature in different areas, including the axilla, tonsil, lung, rectum, meninges, prostate, parotid gland, and tongue.[9] Tumors with similar morphological and immunohistochemical features have also been reported in soft tissues and vaginas with the term mammary-type MFB.[5] Similar molecular findings have also been observed in other benign tumors, such as spindle cell lipoma of soft tissues and cellular angiofibroma of the lower female genital tract, supporting the hypothesis that all these myofibroblastic neoplasms are likely to arise from a typical precursor cell.[10]

Myofibroblasts play an essential role in response to tissue injury. Damaged cells and some malignant tumor cells produce cytokines, notably transforming growth factor β1, causing fibroblasts to migrate into the injured tissue. They begin to develop smooth muscle actin fibers and are transformed into myofibroblasts with the contractile ability.[8] Microscopically, myofibroblastoma of the breast is well demarcated from the adjacent parenchyma, forming a pseudo-capsule.[11] The average size at diagnosis is around 3 cm; however, larger sizes have also been reported,[9] as in our case, measuring 4 cm. Cytogenetic studies have shown that MFB exhibits chromosome 13 rearrangements. In most cases, it was associated with the 13q14 deletion that includes the loss of RB1 or FOXO1 loci.[12] Molecular testing was not performed in our case.

The principal differential diagnosis includes mesenchymal tumors that can arise primarily in the breast parenchyma, such as leiomyoma, spindle cell lipoma, solitary fibrous tumor, spindle cell sarcoma, nodular fasciitis, desmoid-type fibromatosis, angiomyolipomas, angiomyofibroblastoma, pseudoangiomatous stroma hyperplasia and spindle cell carcinoma.[13] The tumor is negative for S-100, which is typically positive at Schwannoma and spindle cell lipoma. Morphology of tumor cells and immunohistochemical positivity for α-smooth muscle actin, desmin, vimentin, and CD34 align with myofibroblastic differentiation of the tumor. In contrast, positivity for h-Caldesmon suggests leiomyomatosis differentiation.[14] Immunohistochemically, myofibroblastoma is positive for vimentin and CD34 and variably positive for desmin and SMA. It is also positive for CD10, CD99, estrogen, progesterone receptors, and BCL-2 protein and only focally positive for h-caldesmon. S100 protein, HMB-45, epithelial markers (EMA and pancytokeratins), and C-kit (CD117) is consistently negative.[8]

This type of tumor causes differential diagnostic problems by mammography and ultrasonography, as it appears in several different variations and, for example, can be confused with hamartoma or fibroadenoma.[6] Mammography usually reveals a single lesion, well delimited, round, or discreetly lobulated.[15] Ultrasonography usually demonstrates a solid circumscribed tumor, although a variable and mixed echo pattern can be expected, sometimes with more distal acoustic attenuation resulting from fat tissue and other types of tissue in the tumor. Doppler modality may show a slight peripheral hypervascularization of the tumor.[16] Radiological imaging is nonspecific in MFB, and pathological examination of needle biopsy

or surgically resected specimen is necessary to diagnose.[5] Diagnostic imaging has revealed its well-demarcated nature; however, various differential diagnoses of other well-circumscribed lesions such as phyllodes tumor, Pseudo Angiomatous Stromal Hyperplasia (PASH), or atypical fibroadenoma should be considered. The point of differentiation is the total absence of epithelial elements in MMF.[4,17]

MMF is a challenging histological diagnosis. Myofibroblastoma is a well-capsulated tumor with a good cleavage plane, which usually allows easy surgical excision. Surgery is the recommended treatment, and relapse is unlikely as long as the resection margins are free. Additionally, malignant transformation has not been reported yet. However, a minimum of 24 months of follow-up is desirable.[6] The accurate diagnosis of MFB is seldom made before histopathology examination and IHC studies. The presence of spindle cells with collagen in the background, low mitotic activity, CD34 positivity, and negative pan-cytokeratin on IHC are the characteristic features of this tumor. As a scarce tumor, the correct diagnosis and prompt management are essential and require careful clinical and pathological workup and extensive sectioning after surgical excision to demonstrate the presence or absence of necrosis, mitosis, or nuclear atypia, and thus rule out a malignant neoplasm.[18]

There have been <100 case reports of mammary MFB reported to date after being first described as a distinct entity in 1987.[7] We add a new case of mammary myofibroblastoma to the limited literature on this uncommon tumor. We hope that this report raises awareness of this tumor and that continued investigation drives further development of efficacious diagnosis and safe treatments for improving patient outcomes.

Figures:

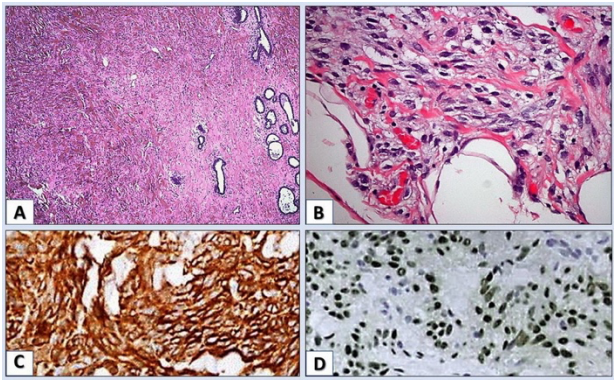

Figure-1: Pathological examination of the excised breast Myofibroblastoma
1A: Low power view showing bundles and fascicles of bland spindle cells in the background of dense collagenous stroma (H&E stain X 20).
1B: High power view showing bland spindle cells, some with focal nuclear enlargement, but rare mitotic activity and no necrosis (H&E stain X 40).
1C: Tumor cells strongly positive for CD34.
1D: Tumor cells positive for Estrogen.

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