Original Article

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Breast Myofibroblastoma: A Single Institutional Case Series

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ABSTRACT

Objective: Breast myofibroblastoma (BM) is a rare, benign mesenchymal tumor primarily affecting older men and postmenopausal women. This study analyzed the clinicopathologic features, immunohistochemical profiles, and treatment outcomes of five BM cases diagnosed at a single institution over a period of 20 years.

Materials and Methods: A retrospective review was conducted for five patients diagnosed with BM between 1998 and 2024. Data included age, clinical presentation, tumor size, histopathologic findings, immunohistochemical profiles, treatment approaches, and follow-up outcomes.

Results: The median age at diagnosis was 68 years, with a mean tumor size of 5.06 cm. Clinical presentation included palpable, painless masses in two patients and an incidental finding in one, while data were unavailable for two cases. Histopathology showed well-circumscribed, unencapsulated tumors composed of spindle cells with admixed adipose tissue and collagen bundles. Immunohistochemically, all tumors were positive for desmin and CD34, with variable smooth muscle actin expression and negative S100 staining. No cases exhibited nuclear beta-catenin staining or 13q14 deletions. All patients underwent surgical excision, with one requiring re-excision due to tumor abutting margins. No recurrences were observed during follow-up (2–18 months).

Conclusion: BM is a benign tumor with favorable outcomes following surgical excision. This study underscores the variability in immunohistochemical staining and the importance of distinguishing BM from other spindle cell tumors. Increased numbers of published cases and refining diagnostic markers may be important to improve clinical management and reduce diagnostic uncertainty.

Keywords: Breast; myofibroblastoma; RB1 deletion; spindle cell tumor

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Key Points

- Breast myofibroblastoma is a rare, benign mesenchymal spindle-cell tumor.
- Imaging characteristics vary; biopsy is required for definitive diagnosis.
- Histologically, tumors are well-circumscribed, unencapsulated, with myofibroblastic differentiation, mostly positive for CD34 and desmin.
- Must be distinguished from other spindle cell tumors.
- Limited numbers of reported cases highlight the need for further study.

Introduction

Breast myofibroblastoma (BM) is a rare benign mesenchymal tumor predominantly seen in older men and postmenopausal women (1). Clinically, it presents as a painless, mobile mass, typically measuring 1–4 cm in size (2). Mammographically, BM often appears as a sharply circumscribed, round or ovoid, non-calcified mass (3). However, there is considerable variability in mammographic appearance, and image-guided biopsy is needed to establish a diagnosis. Histologically, these tumors are well-circumscribed and unencapsulated with myofibroblastic differentiation within a myxoid stroma; notably there is minimal atypia (Figure 1) (2). The diagnosis is confirmed via histopathology, revealing unencapsulated spindle cells with fibroblastic and myoblastic differentiation. This study examined five cases of BM from 1998 to 2024, with a focus on clinicopathologic features, immunohistochemical staining patterns, and treatment outcomes.

An important aspect of diagnosing benign spindle cell lesions in the breast is recognizing the overlap between myofibroblastoma and other entities, such as simple leiomyomas. Both tumors can demonstrate spindle cell morphology and express markers, such as desmin and smooth muscle actin (SMA); however, CD34 expression

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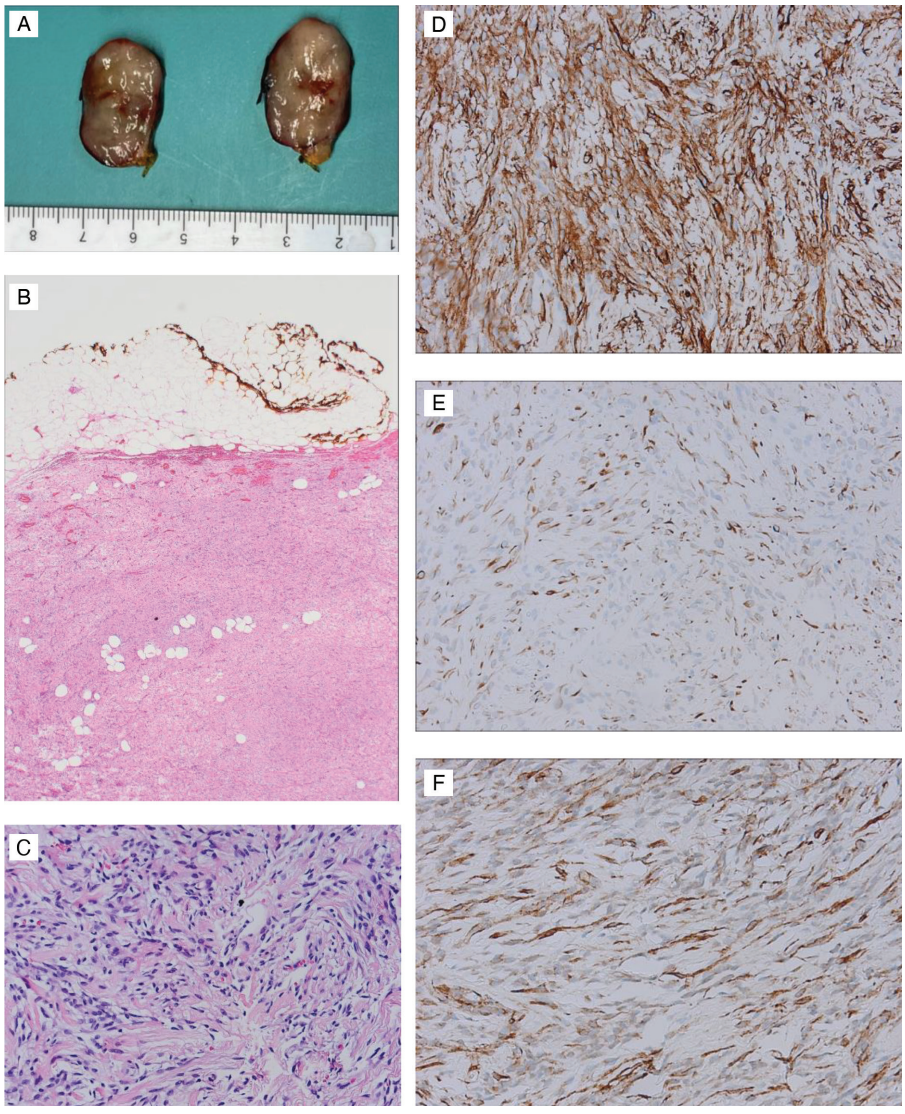

Figure 1. Gross and microscopic pathology of breast myofibroblastoma

A. Well-circumscribed homogeneous tan colored mass lesion. B. Low power photomicrograph highlights a well circumscribed spindle cell lesion containing fat, C. Higher power image highlighting bland appearing spindle cells with blunt ends arranged in fascicles, hematoxylin & eosin stain, 600x. The lesional cells are positive for CD34 (D), desmin (E) and smooth muscle actin (F) by immunohistochemistry, 600x

is a key differentiator, as myofibroblastomas typically express CD34 while leiomyomas do not (4-6). Nonetheless, there are documented exceptions where leiomyomas can express CD34, complicating the differential diagnosis (6). This overlap reflects the broader diagnostic challenge posed by the spectrum of myofibroblastic and smooth muscle differentiation in breast lesions.

The Armed Forces Institute of Pathology (AFIP) classification supports the concept of a spectrum of benign spindle cell lesions with overlapping myofibroblastic differentiation, underscoring the difficulty in drawing clear histological boundaries in many cases (7). These diagnostic challenges are further compounded by the embryologic origin of breast stromal components, which include both myoepithelial and smooth muscle lineages (8). Consequently, some tumors may exhibit hybrid features that defy precise classification, leading to potentially clinically irrelevant subclassifications.

Considering these diagnostic ambiguities, it is essential to approach such cases with a broader perspective that prioritizes clinical management and prognostic relevance over rigid histological labels. The use of ancillary studies such as fluorescent *in situ* hybridization (FISH) for 13q14 deletions, immunostains for retinoblastoma (Rb) protein, and STAT6 expression can aid in narrowing the diagnosis, but do not always resolve the ambiguity fully (5, 7, 9). Our case series, consistent with the AFIP perspective, supports an inclusive approach to categorizing benign spindle cell tumors of the breast as part of a morphologic and immunophenotypic continuum.

Materials and Methods

The medical records of five patients diagnosed with BM between 1998 and 2024 were retrieved from our hospital database and we ascertained the age at diagnosis, presenting symptoms, mode of detection, tumor size and location, radiographic characteristics, surgical treatment, histopathologic features and follow-up outcomes.

Results

There were five cases during the period of the study. The median age was 68 years with a mean of 65.2 years. All patients underwent primary resection without adjuvant therapies, and no recurrences were noted during a follow-up period ranging from 2–18 months. Two patients presented with a painless palpable mass, one presented with an incidental finding on a computed tomography scan, and mode of presentation was not documented for two cases. Tumor sizes ranged from 0.9 cm to 12.5 cm, with a mean size of 5.06 cm and a median size of 2.8 cm (Table 1). All lesions were well circumscribed and composed of fascicles of spindle cells with admixed adipose tissue. The spindle cells were cytologically bland with blunt ends, intersected by bundles of collagen. No significant nuclear atypia, mitoses or necrosis were seen in any of the cases. The majority of the tumors were positive for desmin and CD34 and negative for S100 (Table 2). Two tumors stained positive for SMA, two were negative, one unknown. No evidence of nuclear beta-catenin staining was seen. None of the five cases tested positive for 13q14 deletion. Following primary resection, one patient had tumor abutting resection margins and underwent re-excision of the lumpectomy cavity. No recurrences were noted during the variable follow-up periods. None of the patients received adjuvant radiation or systemic treatments.

Discussion and Conclusion

BM is a rare, benign, mesenchymal tumor originating from stromal cells and accounting for less than 1% of all breast tumors (10). It predominantly affects middle-aged to elderly individuals, with a slight male predominance (11). Libbrecht et al. (11) report that these lesions most commonly occur in individuals in their fifth and sixth decades of life. Typically, the tumor presents as a painless, well-circumscribed, mobile mass in the breast, often discovered incidentally during self-examination or routine mammography (10). Our physical exam mirrors what is seen in earlier publications about BM, where patients presented with a painless lump identified during self-examination.

Table 1. Clinical features of five cases of breast myofibroblastoma

Case number	Age	Laterality	Tumor size (cm)
1	51	Right	2.8x2.5x1.8
2	76	Left	1.1x1x0.7
3	61	Right	8.0x7.0x2.5
4	70	Right	12.5x11.8x5.7
5	68	Right	0.9x0.8x0.3

Table 2. Immunophenotype of five cases of breast myofibroblastoma

Case number	CD34	SMA	Desmin	S100
1	+	+	+	Unknown
2	+	+	+	-
3	Unknown	Unknown	Unknown	Unknown
4	+	-	+	-
5	+	-	-	-

SMA: Smooth muscle actin

The pathogenesis of BM is thought to involve several mechanisms. Chromosomal abnormalities, particularly deletions and rearrangements involving chromosomes 13q14 and 17, play a central role in tumor formation (4). Deletions within the 13q14 chromosomal region, including genes such as *RB1* and *FOXO1A*, disrupt cell cycle regulation and apoptosis, contributing to tumor growth (9, 12). Loss of heterozygosity at 13q14 and reduced Rb protein expression are critical features in the disease's progression (13). These genetic abnormalities are also seen in related tumors, such as spindle cell lipomas and cellular angiofibromas, suggesting a shared histogenetic origin (9). Advanced diagnostic tools, such as FISH and immunohistochemical analysis for Rb protein assist in identifying these alterations and distinguishing myofibroblastomas from other spindle cell tumors of the breast (4, 5, 14).

Histologically, BMs consist of randomly arranged fascicles of spindle-shaped cells mixed with adipocytes in a collagenous and myxoid background, consistent with our findings (6). Immunohistochemical studies typically show positivity for CD34, desmin, and SMA, and negativity for S100 and beta-catenin (1). However, certain variants may not display CD34 and desmin expression, which can complicate the diagnostic process (5). The expression of these markers helps distinguish myofibroblastoma from other spindle cell tumors, like schwannomas, malignant peripheral nerve sheath tumors, and synovial sarcomas (7). Among our five cases, three tumors were positive for desmin, one was negative (Patient 5), and one result was unavailable (Patient 3). CD34 was positive in four cases; the result for Patient 3 was unknown. SMA was positive in two cases, negative in two, with Patient 3 again being unknown.

The distinction between myofibroblastoma and leiomyoma remains particularly challenging. Leiomyomas, while typically negative for CD34, may exhibit focal positivity in rare instances, and show stronger and more diffuse desmin and SMA staining than myofibroblastomas. Yet, these immunophenotypic nuances may not always translate into clinical significance. Therefore, in cases where histologic and immunohistochemical features are equivocal, it may be more appropriate to emphasize the benign nature of the tumor and exclude malignancy, rather than overemphasize its precise nomenclature (4-7).

BMs are generally treated with wide local excision, without administration of radiotherapy or systemic therapy. In our series, the mean diameter of excision was 5.06 cm, consistent with what is reported in the literature. Imaging studies, such as mammography and ultrasound, are often used to help characterize these breast lesions but defining and distinguishing myofibroblastomas from other conditions remains challenging. Radiographic evaluations of myofibroblasotmas, including those by Magro et al. (9) often show benign features, with the tumors being incidentally found during examination for other symptoms (15).

Given its rarity, with less than 100 cases reported since its first description in 1987, each new case of BM significantly contributes to the understanding of this tumor. The importance of identifying additional cases of BM stems from the necessity to differentiate it from other breast lesions. Differential diagnosis of spindle cell lesions of the breast that diffusely express CD34 include myofibroblastoma, solitary fibrous tumor, pseudoangiomatous stromal hyperplasia (PASH) and dermatofibrosarcoma protruberans (DFSP). Solitary fibrous tumors share some morphologic features with myofibroblastoma with regards to spindle cell cytomorphology; in addition, they show prominent staghorn like vasculature, lack muscle markers and most importantly, express STAT6 by immunohistochemistry. PASH is a lesion of

myofibroblastic origin, and hence, will have immunophenotypic overlap with myofibroblastoma. However, PASH is morphologically distinct, forming slit like clefts in the stroma. DFSP is a cutaneous based, locally aggressive, spindle cell tumor with a storiform pattern of growth, poorly defined margins, lacks muscle marker expression, and is often positive for platelet-derived growth factor beta rearrangement, detectable by FISH. Therefore, expanding the pool of documented cases of BM will aid in establishing distinct diagnostic criteria and refining differential diagnoses to ensure appropriate clinical management. Our case series aims to enhance the differential diagnosis and reduce misdiagnosis.

In the context of breast cancer research, advanced genomic technologies, such as next-generation sequencing, hold significant potential for elucidating the molecular composition of BM. These approaches may offer valuable insights into its genetic aberrations, associated signaling pathways, and potential therapeutic targets. Prior studies have emphasized the impact of genetic predisposition on disease susceptibility, with *BRCA1* and *BRCA2* mutations being well-established risk factors for hereditary breast cancer. While BM is not typically associated with genetic predisposition or hereditary syndromes, exploring the genetic composition of this tumor could reveal novel genetic alterations or loci that contribute to its development. The collection of additional cases and further exploration of advanced techniques will be important to enhance diagnostic accuracy, optimize treatment strategies, and improve overall patient care.

Study Limitations

Our findings aligned with the existing but limited literature on BM, further demonstrating its benign nature and favorable prognosis following surgical excision. The variability in immunohistochemical staining highlighted the need for continued study to refine diagnostic markers. This study adds to the limited body of literature on BM, contributing to the differentiation of BM from other spindle cell tumors of the breast, such as phyllodes tumors and fibroadenomas, ensuring accurate diagnosis and appropriate treatment.

In conclusion, BM represents a unique entity among benign spindle cell tumors. Increased numbers of published cases, refining diagnostic markers and applying advanced molecular profiling techniques may aid in producing consensus diagnostic criteria and treatment guidelines, ultimately resulting in better care for individuals affected by this rare tumor.

Ethics

Ethics Committee Approval: Not necessary.

Informed Consent: Not necessary.

Footnotes

Authorship Contributions

Concept: A.N., I.J.; Design: A.N., I.J.; Data Collection or Processing: M.P., M.G.P., V.R., A.N.; Analysis or Interpretation: M.P., M.G.P., V.R., A.N., I.J.; Literature Search: M.P., M.G.P., V.R., A.N., I.J.; Writing: M.P., M.G.P., V.R., A.N., I.J.

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