Mammary Myofibroblastoma

A Tumor With a Wide Morphologic Spectrum

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• ***Context.*—Myofibroblastoma (MFB) of the breast is an unusual benign tumor that belongs to the family of the "benign spindle cell tumors of the mammary stroma." The name MFB reflects its cellular composition, comprising mainly stromal cells with fibromyofibroblastic and, less frequently, myoid differentiation. Since the original description, the morphologic spectrum of MFB has been expanded by the recognition of several unusual morphologic variants, such as the cellular, infiltrative, epithelioid, deciduoid-like, lipomatous, collagenized/fibrous, and myxoid variants.**

***Objective.*—To review the literature on mammary MFB, discussing the main clinical, radiologic, and pathologic features helpful for diagnosis. Since MFB may show alarming morphologic features, which can lead to a misdiagnosis of malignancy, histologic figures of this tumor, including its more unusual variants, are provided to offer pathologists a practical approach to a correct diagnosis. Histogenesis and pathogenesis of this tumor are also proposed.**

***Data Sources.*—Clinicopathologic data on MFB were extracted from all identified articles through PUB Medline–based research. Histologic figures have been taken from the personal archive of the author.**

***Conclusions.*—The incidence of MFB diagnosis has increased in recent years, likely due to the mammographic screening. Accordingly, this unusual benign tumor may represent a potential diagnostic pitfall, especially when interpreting fine-needle aspiration and/or needle core biopsy. Pathologists should be aware of the wide morphologic spectrum exhibited by MFB to avoid a misdiagnosis of malignancy.**

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The benign stromal tumors of the mammary stroma encompass a wide spectrum of lesions sharing so many basic common clinical, morphologic, and immunophenotypic features that their recognition as a distinct entity is warranted.[1–3] Several similarities between these neoplasms and the stromal tumors arising from the lower female genital tract (ie, superficial myofibroblastoma, angiomyofibroblastoma, cellular angiofibroma) have recently been emphasized.[3] Myofibroblastoma (MFB) is the prototypic tumor of the mammary stroma,[1–4] comprising neoplastic cells showing a variable fibromyofibroblastic differentiation at morphologic, immunohistochemical, and ultrastructural levels.[1,2,4–9] It is typically a bland-looking spindle cell tumor exhibiting expression of vimentin, desmin, and CD34 in most cases.[1–3] Until now, approximately 70 cases of mammary MFB have been reported in the English language literature.[10] However, the first cases of a benign spindle cell stromal tumor of the breast were reported by Toker et al[11] in 1981. These authors reported 4 cases of breast tumors with morphologic features similar to spindle cell lipoma of soft tissue, and they classified them with the descriptive term of *benign spindle cell tumor of the breast*.[11] Similar breast tumors were later reported with different names, including *benign spindle cell tumor of the male breast,*[12] *spindle cell lipoma,*[13–15] or *fibroma.*[15] All of these lesions likely represent the herald of the postcoming tumors labeled MFBs. The term *myofibroblastoma of the breast* was first coined by Wargotz et al in 1987,[4] who proposed that such a tumor represents a distinct clinicopathologic entity. Although MFB seemed to be an appropriate name for such a tumor, some authors generated a list of less popular terms, such as *myogenic stromal tumor,*[16] *solitary fibrous tumor,*[17] or *atypical variant of leiomyoma,*[18,19] for similar, if not identical, lesions.

CLINICAL FEATURES

Myofibroblastoma was originally described as a typical tumor occurring in the breast of adult males.[4] Subsequently, several cases were also documented in females, suggesting that it can occur in both sexes.[1,2,6,7,20–23] It is likely that the increased incidence of MFB reported in women in the last 2 decades could be due to increased mammographic screening.[7,24,25] Currently, it is believed that MFB occurs mainly in older men and postmenopausal women.[24] The patients are adults and range in age at presentation from 25 to 87 years,[2,26] with only 1 case described in an adolescent boy[27] and no pediatric case so far described. As mammary MFB has been reported in multiple races,[1,2,4,10,25,28–30] it seems to have no predilection for any particular race. Although MFB is a tumor occurring sporadically, without a known genetic predisposition or association with other diseases, in a limited number of cases it has been documented in the setting of gynecomastia[4,5,26,31] or androgen ablation therapy for prostatic cancer.[24] Moreover, single cases of MFB have been reported arising at the site of a surgical scar for breast cancer removal[6] or in a breast treated with radiation therapy for an in situ carcinoma[32] or in association with an invasive carcinoma.[8] In 1 case, a history of trauma to the chest wall was documented.[33] Two patients with MFB had a coincidental carcinoma of the pancreas and kidney, respectively.[8] Physical

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examination discloses a solitary, unilateral, painless, freely movable, usually firm in consistency, nontender nodule that has been growing slowly during the course of several months to years.[1,2,4,5] More rarely, patients complain of massive enlargement of breast due to a giant tumor[5,30,34,35] clinically suspected to be a phyllodes tumor.[30] In some cases, MFB has been detected as a nonpalpable mass on a routine screening mammogram.[25,36] Synchronous bilaterality and unilateral multicentricity have rarely been documented.[21] Local excision is curative, with no evidence of recurrence or distant metastasis after a follow-up period of 15 years.[2]

RADIOLOGIC FEATURES

Ultrasonography confirms the solid nature of the tumor, showing a well-circumscribed, homogeneous, slightly hypoechoic mass[2,34,36–41] suggestive of fibroadenoma. Mammographic findings usually consist of a well-circumscribed, round to oval, dense mass, variable in size, frequently 1 to 4 cm in its greatest diameter,[2,8,24,36–42] and devoid of calcifications. Rarely, the nodular mass may show coarse calcifications within tumor.[37] Magnetic resonance, in the few cases it was performed, revealed a well-circumscribed nodular mass with homogeneous enhancement and internal septations.[39]

PREOPERATIVE DIAGNOSIS

Myofibroblastoma can be suspected on fine-needle aspiration cytology (FNAC).[44–50] The aspirates usually consist of randomly arranged, single and/or clustered oval- to spindle-shaped cells[43–45,47,50] occasionally showing nuclear pleomorphism.[46] Although the diagnosis of MFB can be rendered on FNAC if cytologic findings are evaluated in conjunction with the clinical and radiologic data,[42,46,48] it remains ambiguous in some cases,[45,51] with a misdiagnosis of gynecomastia or phyllodes tumor or malignancy.[8,49] An ultrasound-guided core biopsy increases the chance of a correct preoperative diagnosis of MFB.[34,36,40,42] However, it can be difficult in some cases, especially if the pathologist is faced with unusual morphologic variants showing worrisome features (ie, MFB with atypical cells, epithelioid MFB, myxoid MFB with or without atypical cells, lipomatous MFB, and deciduoid-like MFB).[2,8]

PATHOLOGIC FINDINGS

Macroscopic Features

Tumor size ranges from a few millimeters to 11 cm.[35] By gross examination, MFB is generally a well-circumscribed, firm and rubbery, unencapsulated, round to oval mass. The cut surface usually reveals a solid lesion, with a smooth or lobulated external surface, pale white to grayish, with a variably whorling appearance.[1,5,22,24,29,35,43] In some cases, the cut surface of tumor may show focal to extensive mucoid- or lipomatous-appearing areas.[2,3,5,35,52] Cystic degeneration, necrosis, and hemorrhage are not features of MFB.

Histologic Features

Although MFB is typically a bland-looking spindle cell tumor, there is increasing evidence that it encompasses a morphologic spectrum wider than originally described.[4] This is mainly due to the fact that neoplastic cells, showing a variable fibro-myofibroblastic differentiation, may adopt marked intralesional and interlesional variability in morphology.[1,2,4] Accordingly, several histologic variants (cellular, infiltrative, epithelioid, deciduoid-like, collagenized/fibrous, lipomatous, myxoid variants), including some unusual features, have been recognized in the last 2 decades. Their recognition is crucial to avoid confusion with other benign or malignant breast tumors. Despite the fact that MFB may exhibit a wide morphologic variation in cellular composition, growth patterns, and extracellular matrix, it maintains a basic common theme, the recognition of which is crucial for a correct diagnostic interpretation (Table 1).

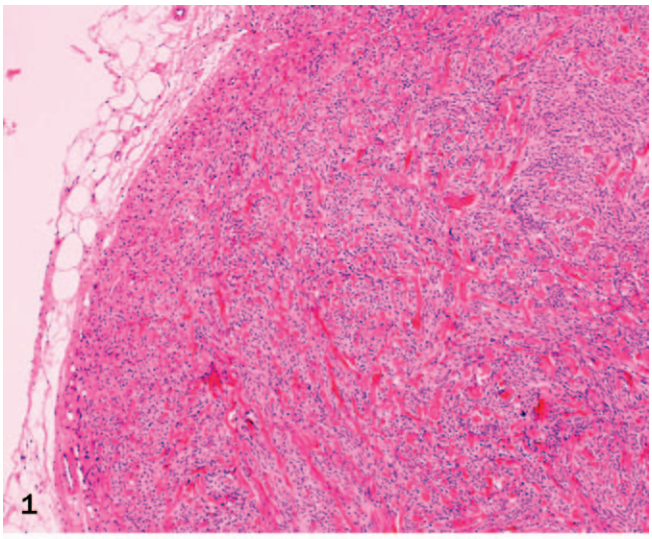
Table 1. Morphologic Features Helpful for Diagnosis of Myofibroblastoma

Essential diagnostic criteria
Purely mesenchymal tumor with no epimyoepithelial components
Interspersed thick, hyalinized collagen bundles
Low mitotic count (0–2 mitoses per 10 high-power fields)
No atypical mitoses
No necrosis
Intratumoral or intertumoral variations
Cell types: spindle-shaped and oval- to epithelioid-shaped cells; more rarely, deciduoid-like cells
Cytologic atypia: absent; mild; more rarely, moderate to focally severe
Growth patterns: fascicular, nesting, solid; rarely, alveolar, trabecular, or single-file patterns
Tumor stroma: myxoid to hyalinized fibrous stroma
Tumor borders: pushing borders; rarely, infiltrative borders
Additional tumor components: adipose tissues; more rarely, cartilaginous, smooth muscle, osseous tissues

Classic-type MFB is an unencapsulated tumor with a pushing, lobulated growth pattern, usually composed of bland-looking, slender, spindle-shaped cells, closely packed in short, straight, haphazardly intersecting fascicles or clusters of cohesive cells, interrupted by thick, hyalinized collagen bundles (Figures 1 and 2). A minority of cases may show invasive margins with a small amount of entrapped mammary glands.[8] Although amianthoid-like collagen bundles are a typical feature of intranodal MFBs,[53] they are seen less frequently in mammary tumors.[1,2,4,5,52,54] The cells vary their appearance, ranging from fibroblastic-like cells with scanty cytoplasm and elongated nuclei to cells with overt myoid features consisting of abundant palely to deeply eosinophilic cytoplasm (Figure 2). The latter cells have distinct cell borders and contain round to oval nuclei with 1 or 2 small nucleoli (Figure 2). Occasionally, nuclei may have grooves or pseudoinclusions.[4,5,22,43] In some areas, neoplastic cells may exhibit a palisading of nuclei, closely mimicking a benign peripheral nerve sheath tumor.[1,2,5] Mitoses are absent or numbered up to 2 per 10 high-power fields.[1,2,4,6] The tumor vascular component is variably represented by small- to medium-sized vessels frequently showing hyalinization and foamy histiocytes in their walls.[1,2,5,55] Generally, numerous mast cells can be found in tumor stroma,[1,2,4,5,49] whereas a lymphoplasmacytic infiltrate is absent or only focally detected.

Morphologic Variants

Cellular MFB.—Cellular variant is characterized by a dense proliferation of spindle-shaped cells, focally showing nuclear overlapping, with interspersed hyalinized collagen bundles, usually smaller in size than those seen in classic MFB (Figure 3). This variant may show a mild cellular pleomorphism, a focal storiform or herringbone pat-



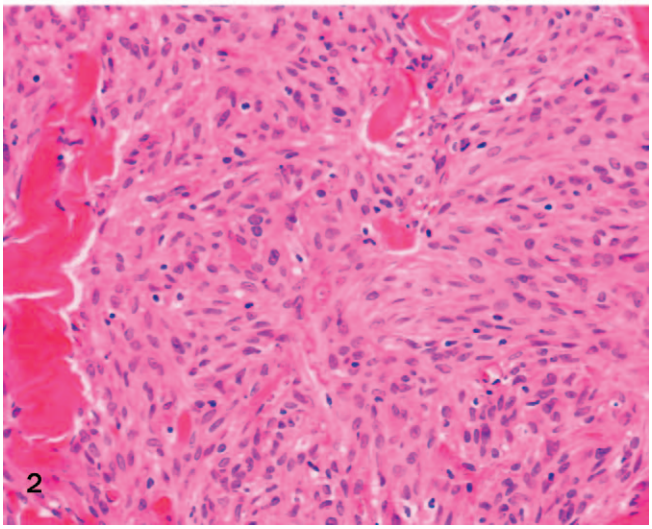
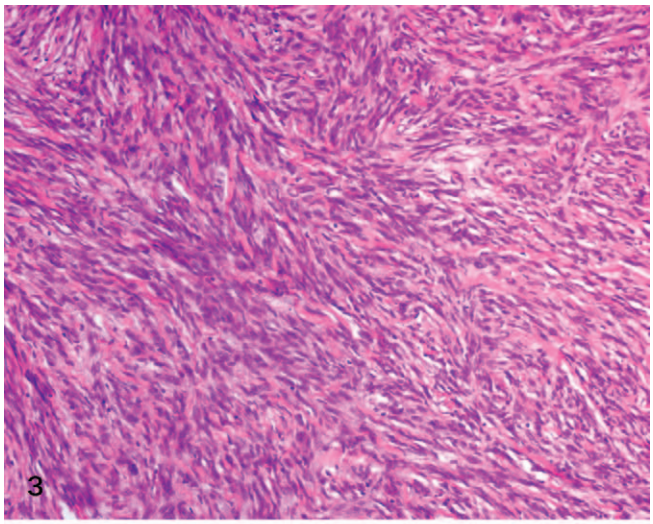
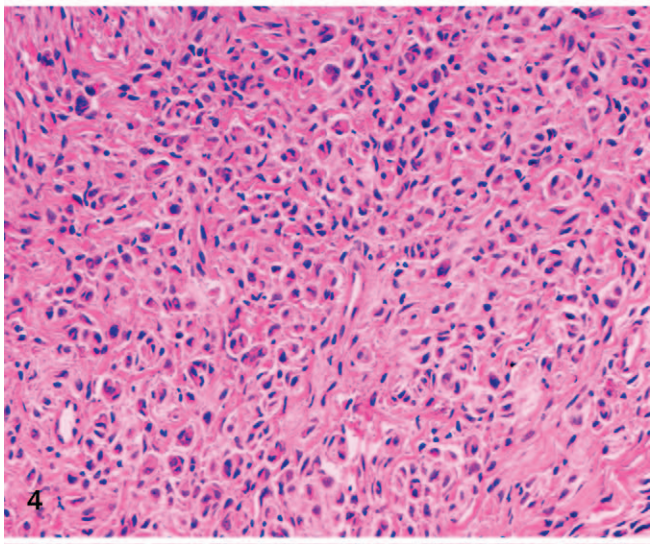


Figure 1. *Myofibroblastoma, classic type. Low magnification showing a fascicular tumor with pushing borders and numerous interspersed thick, hyalinized collagen bundles (hematoxylin-eosin, original magnification ×50).*

Figure 2. *Myofibroblastoma showing bland-looking, spindle-shaped cells with a myoid appearance. Small nucleoli are evident. Although this tumor is morphologically and immunohistochemically (desmin and focally α-smooth muscle actin positivity) reminiscent of leiomyoma, it contains thick, eosinophilic collagen bundles and is diffusely stained with CD34, CD10, bcl-2, and CD99 and only focally to h-caldesmon (hematoxylin-eosin, original magnification ×200).*





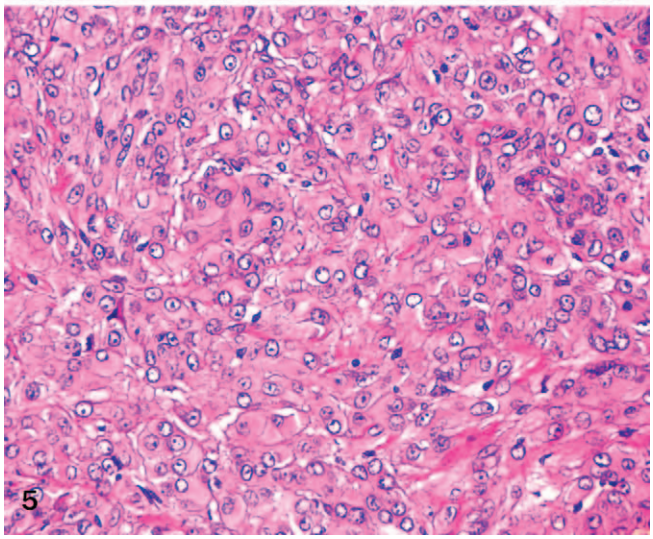


Figure 5. *Myofibroblastoma, deciduoid-like variant. This tumor is composed exclusively of large-sized, eosinophilic, deciduoid-like cells with large vesicular nuclei containing 1 or 2 prominent nucleoli. The tumor is reminiscent of an apocrine carcinoma (hematoxylin-eosin, original magnification ×200).*

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Figure 3. *Myofibroblastoma, cellular variant. Hypercellular tumor with fibroblast-like appearance. Neoplastic cells are arranged in intersecting fascicles and intermingle with eosinophilic collagen bands (hematoxylin-eosin, original magnification ×100).*

Figure 4. *Myofibroblastoma, epithelioid variant. This tumor is composed of mononucleated and binucleated or multinucleated eosinophilic epithelioid cells with nuclear pleomorphism, arranged either as single cells or in small clusters. Eosinophilic collagen bands are interspersed among cells (hematoxylin-eosin, original magnification ×200).*

tern and tends to have infiltrative borders microscopically.[6,8,47]

Infiltrating MFB.—Occasionally, MFB exhibits an extensive invasive growth pattern, entrapping fat and/or mammary glandular structures.[8,21,47,56,57] This infiltrative growth pattern is reminiscent of that seen in fibromatosis.

Epithelioid MFB.—Classic-type MFB may contain a minority of epithelioid cells,[2,3,6,21,48,58] either isolated or in clusters. Accordingly, the term *epithelioid MFB* should be reserved to those tumors composed exclusively or predominantly (>50%) of epithelioid cells.[2,3,7,8,21,23] In these cases, medium-sized mononucleated, binucleated, or multinucleated neoplastic cells with well-defined cell borders are oval to polygonal, with abundant eosinophilic cytoplasm and round to oval, eccentrically placed nuclei containing small evident nucleoli (Figure 4). Epithelioid cells are usually arranged in clusters or in alveolar, solid, or trabecular growth patterns, and they are variably embedded in a myxoid to fibrous stroma.[2,3,8,48] Hyalinized collagen bundles of varying size are usually detected among neoplastic cells (Figure 4). A single cell file arrangement, as seen in invasive lobular carcinoma, can be observed.[1,2] Immunohistochemistry is helpful for confirming diagnosis.

Deciduoid-like MFB.—Recently, 1 case of MFB composed exclusively of cells that adopt a deciduoid-like morphology has been recognized.[54] These large-sized cells, arranged in nests or in solid or trabecular patterns, are round to ovoid to polygonal, with abundant eosinophilic glassy cytoplasm and sharp cellular borders. Nuclei are large and round, with vesicular chromatin containing a single or multiple prominent nucleoli (Figure 5). These cells have an overall appearance reminiscent of decidua.[54] Numerous cells are binucleated. Occasionally, some cells showing eccentric nuclei and spherically eosinophilic intracytoplasmic inclusions, are reminiscent of rhabdoid cells.[54] Thick, eosinophilic collagen bundles, sometimes with an amianthoid-like appearance, are frequently observed among cells or around cellular nests. At the morphologic level, the cells of this variant look like those described in the ''deciduoid-like stromal changes'' observed in the setting of gynecomastia in a diabetic patient.[59] Immunohistochemistry is crucial for a correct diagnosis and in ruling out malignancy.

Lipomatous MFB.—Myofibroblastoma may contain a variable amount, with generally small foci, of adipose tissue as integral tumor component.[1–3,5,8,9,60] However, only the cases that are composed predominantly (>75% of the entire neoplasm) of a fatty component merit the name of *lipomatous MFB* (Figure 6).[61,62] Adipocytes are uniform in size and shape and lack nuclear pleomorphism. Lipoblasts are absent. The basic tumor spindle cell component shows a fingerlike growth pattern toward the fatty component, resulting in a fibromatosis-like appearance (Figure 6).[61] The spindle cells may exhibit a mild to moderate nuclear pleomorphism.

Collagenized/Fibrous MFB.—In the collagenized or fibrous variant, the spindle cells are distributed in a highly collagenous stroma (Figure 7).[2,3,6,8,51] The thick, hyalinized collagen bundles, typical of classic MFB, are reduced in number. Instead, irregular slitlike spaces, resembling those seen in pseudoangiomatous stromal hyperplasia, can be identified between tumor cells (Figure 8).[8]

Myxoid MFB.—Focal myxoid stromal changes are common in MFB.[2,3,8,42,55] However, the term *myxoid MFB* should be reserved to those lesions entirely or predominantly consisting of myxoid stroma in which spindle- and stellate-shaped cells are embedded (Figure 8).[8,35,52] The typical thick, hyalinized collagen bundles can be difficult to identify because they are dispersed throughout the myxoid matrix. Cases of myxoid MFB containing predominantly atypical cells with moderate to severe degrees of nuclear pleomorphism have recently been described (Figure 8).[52] Immunohistochemistry is helpful in the diagnosis.

Mixed Variants.—Two or more variants may coexist within the same MFB (ie, epithelioid and lipomatous variants, cellular and epithelioid variants, cellular and collagenized/fibrous variants).[1,2]

Unusual Morphologic Features

Atypical Cells.—Despite the morphologic variant, MFB may contain a variable number of atypical mononucleated or multinucleated cells showing a variable degree (mild to severe) of nuclear pleomorphism.[8,29,45,55,58,60,63,64] This alarming feature is more frequent in the cellular,[47] epithelioid,[2,3,23] myxoid,[52] and deciduoid-like[54] variants (Figures 4, 5, and 8). Single atypical bizarre cells can be encountered in MFB[2,3,55] (Figure 9) and have been regarded as degenerative in nature, similar to what was observed in other benign soft tissue tumors (ie, atypical/symplastic leiomyoma, ancient schwannoma). Occasionally, atypical cells, embedded in a myxoid stroma with microcystic changes, may mimic lipoblasts.[55]

Multinucleated Cells and Multinucleated Floretlike Cells.—Multinucleated cells have been reported in some cases of MFB,[1,4,8,21] especially in the epithelioid variant.[2] Multinucleated floretlike cells, identical to those commonly observed in pleomorphic lipoma, have also been described (Figure 10).[7,55]

Heterologous Components.—Apart from adipose tissue, only rarely may MFB contain, as an integral part of tumor, foci of heterologous mesenchymal components, such as mature leiomyomatous,[8,29,64,65] osseous,[37] or cartilaginous[4,8,29,37,48] tissues, which can variably coexist in the same tumor.[29,37]

Hemangiopericytoma-like Pattern.—A hemangiopericytoma-like pattern can be observed occasionally in MFB.[55] This is not surprising, as many soft tissue neo-

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Figure 6. *Myofibroblastoma, lipomatous variant. Mature adipose tissue comprises more than 75% of the entire tumor. In this area, the spindle cell component, containing interspersed thick, hyalinized collagen bundles, shows a fingerlike pseudoinfiltration into the fatty component. Tumor has pushing margins (hematoxylin-eosin, original magnification ×40).*

Figure 7. *Myofibroblastoma, collagenized/fibrous variant. Hypocellular tumor with a densely hyalinized stroma and thick, eosinophilic collagen fibers. Artefactual slitlike spaces are seen (hematoxylin-eosin, original magnification ×100).*

Figure 8. *Myofibroblastoma, myxoid variant. Tumor is composed predominantly of atypical spindle cells embedded in a highly myxoid stroma. Thick, eosinophilic collagen bands can be detected in the stroma (hematoxylin-eosin, original magnification ×100).*

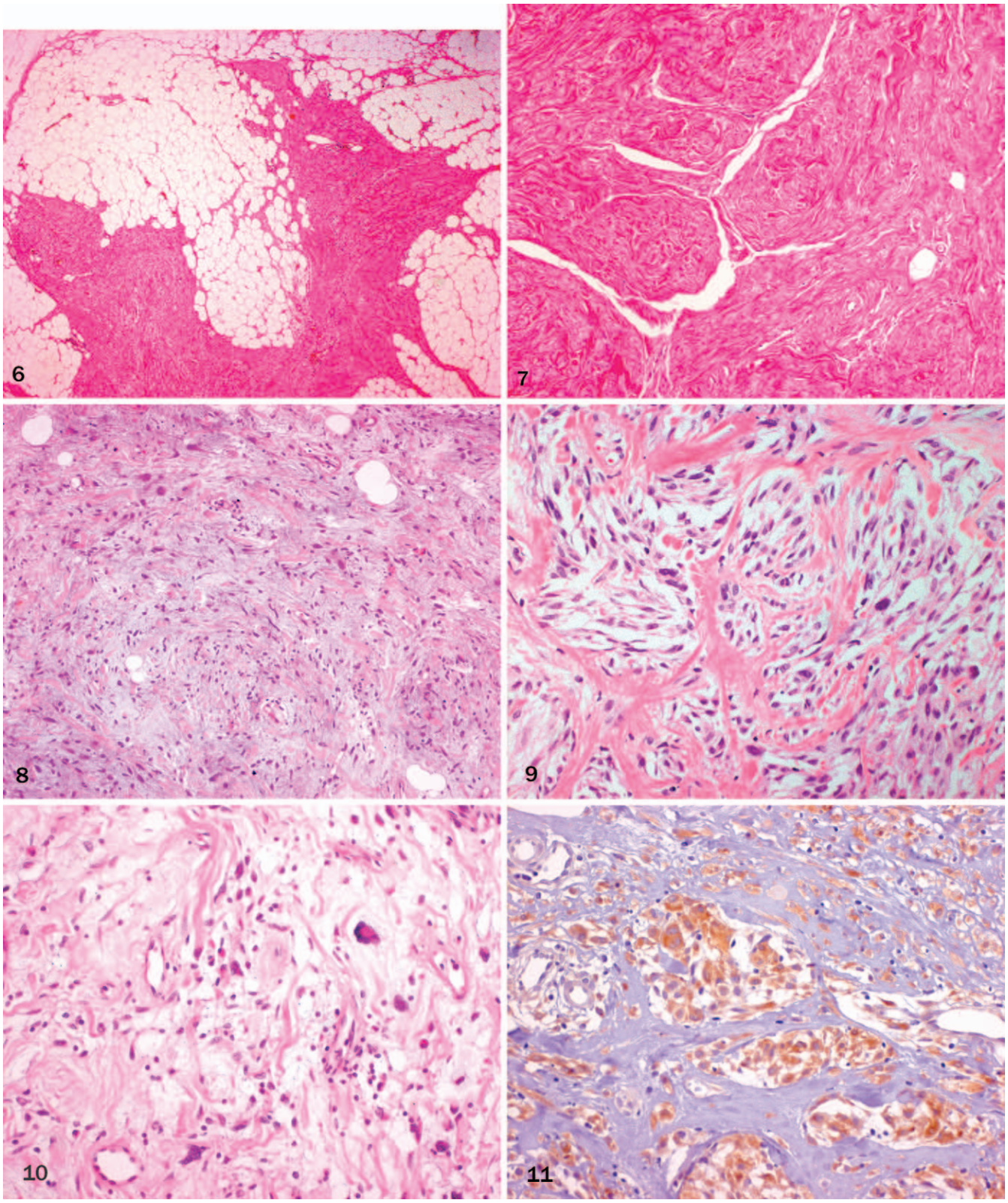

Figure 9. *Myofibroblastoma showing spindle cells with nuclear pleomorphism of mild to moderate degree. Neoplastic cells are arranged in nests surrounded by thick, eosinophilic collagen bundles (hematoxylin-eosin, original magnification ×250).*

Figure 10. *Myofibroblastoma showing a myxoid area with spindle-shaped cells, multinucleated cells, one of which has a floretlike appearance, and eosinophilic collagen bands (hematoxylin-eosin, original magnification ×250).*

Figure 11. *Myofibroblastoma, epithelioid variant. Mononucleated or binucleated polygonal cells, arranged in an alveolar growth pattern, are strongly stained with desmin (diaminobenzidine chromogen, hematoxylin counterstain, original magnification ×250).*

plasms may show a similar growth pattern. This possibility should be kept in mind for differential diagnosis with solitary fibrous tumor.[55]

IMMUNOHISTOCHEMICAL FINDINGS

Most cases of MFB are typically positive to vimentin, desmin, and CD34.[1,2,6,9,20,21,29] Immunoreactivity for α-smooth muscle actin, bcl-2, and CD99 is frequently obtained, but with a variable extension in different tumors and also in different areas of the same tumor.[1,2,4,6,8] CD68 and factor XIIIa immunoreactivity has been documented in some cases.[6,58] Recently, MFB has also been shown to be positive for CD10.[66] A focal expression of h-caldesmon can be encountered in scattered cells.[60] Interestingly, most MFBs are stained with estrogen, progesterone, and androgen receptors.[1,2,67–69] Cytokeratins, EMA, S100 protein, HMB-45, and c-Kit (CD117) are consistently negative. Immunohistochemistry is extremely helpful in confirming the diagnosis of unusual variants of MFB (Figure 11).

ULTRASTRUCTURAL FINDINGS

Electron microscopy studies, performed in some cases of MFB, have shown a variable admixture of undifferentiated mesenchymal cells, fibroblasts, myofibroblasts, and smooth muscle cells. Generally, myofibroblasts are represented by cells rich in organelles (rough endoplasmatic reticulum, Golgi complexes) and containing bundles of myofilaments forming focal densities. Basal lamina-like material is focally identified in association with the cell surface.* Fibronectin fibrils (so-called microtendons) and fibronexus junctions, features typically seen in myofibroblasts isolated from granulation tissue of healing wounds, are only occasionally seen.[6,35]

CYTOGENETIC FINDINGS

Some cytogenetic studies have shown chromosome 13 rearrangements associated with the loss of the 13q14 chromosomal region in 2 cases of mammary MFBs[70] and in 1 case of soft tissue MFB[71]; in one of the mammary cases was also documented a partial loss of 16q.[70] Notably, these chromosomal alterations are typically observed in spindle cell lipoma.[72] The similar cytogenetic profile shared by MFB and spindle cell lipoma, along with their close morphologic, and partially immunohistochemical, overlapping are in favor of a histogenetic link between these two tumors.[1,2,11,24,66]

HISTOGENESIS AND PATHOGENESIS

The evidence that MFB arises from mammary stroma is supported by the evidence that stromal cells, in some nontumoral pathologic conditions, may adopt morphologic features similar to those seen in MFB.[8,73] One of these conditions is the so-called pseudoangiomatous stromal hyperplasia,[8,74] a fibro-myofibroblastic reactive lesion which has been found to be associated in some cases with MFB.[8,21] Notably, stromal myofibroblastoma-like changes have also been observed in pseudoangiomatous stromal hyperplasia,[8] fibro(stromo)epithelial lesions,[73] or in the setting of gynecomastia in a diabetic patient.[57] The detection of mature fatty, smooth muscle, osseous, or cartilaginous components as an integral part of MFB raises additional interesting histogenetic considerations. It has been postulated that benign stromal tumors of the breast, including MFB, arise from a common precursor mesenchymal cell.[1–4,29] The $CD34^+$ uncommitted mammary stromal cells are credited to play a crucial role in the histogenesis of this tumor category,[1–3,58,61] in consonance with their ability to differentiate along several mesenchymal lines, including fibroblastic, myofibroblastic, adipocytic, leiomyomatous, osseous, and cartilaginous.[1,2,61,65] This capability of multilineage differentiation could explain the coexistence of different cytotypes (ie, fibroblasts, myofibroblasts, adipocytes), including some heterologous (ie, smooth muscle, cartilaginous, osseous) ones, in the same MFB.[29,65,75] According to this histogenetic hypothesis, the lipomatous MFB could be viewed as the morphologic result of an unbalanced bidirectional differentiation of the precursor mammary stromal cell, with the adipocytic component overwhelming the myofibroblastic portion.[61] Moreover, the inherent plasticity of mammary stromal cells to undergo changes in their pheno-immunophenotype provides the explanation for the wide morphologic spectrum exhibited by MFB (epithelioid variant, deciduoid-like variant, mixed variants). Although the etiologic factors of mammary MFB are still to be established, a pathogenetic role of sex steroid hormones has been suggested.[67–69] This is supported by the following evidence: (1) most MFBs variably express estrogen, progesterone, and androgen receptors[67–69]; and (2) MFB may be associated with gynecomastia[4,6,31] or pseudoangiomatous stromal hyperplasia,[21] 2 distinct pathologic conditions sharing a hormonal etiology.[8,74,76]

DIFFERENTIAL DIAGNOSIS

With the increasing use of radiologic technology in breast pathology, the possibility to encounter an MFB on FNAC or needle core biopsy will increase. Some authors doubt that a definitive cytologic diagnosis of MFB can be achieved, suggesting that the most important role of FNAC is to rule out malignancy.[45] Needle core biopsy of an MFB can be difficult to interpret, especially if one is faced with unusual variants. Epithelioid MFB, showing cells with an epithelioid morphology, sometimes with nuclear pleomorphism, may be confused with an invasive lobular carcinoma due to its growth pattern in single cell files.[2,3,8] The same diagnostic problems may arise with deciduoid-like MFB, which when exhibiting large atypical cells with vesicular nuclei, may mimic an apocrine carcinoma.[54] Finally, the lipomatous variant of MFB, for its pseudoinfiltration of spindle cells toward the fatty component, could lead to a misdiagnosis of desmoid-type fibromatosis or fibromatosis-like low-grade carcinoma or low-grade sarcoma.[61,62] Immunohistochemistry, showing negative staining with cytokeratins and immunoreactivity with desmin and CD34, and variably with smooth muscle actin, CD99, and bcl-2, helps to exclude carcinoma.[2,3] On the contrary, more caution should be used in the differential diagnosis with fibromatosis or low-grade sarcomas[24] when interpreting small incisional biopsies.[1,2,35] The diagnosis of MFB in a surgical specimen is usually straightforward in most cases by light microscopy alone.[2] However, a differential diagnosis with a wide variety of benign and malignant mammary spindle cell lesions is necessary (Table 2). Generally, the lack of marked cytologic atypia, along with an absence of necrosis, high mitotic activity, and atypical mitoses, are helpful features to exclude malignancy. The morphologic and immunohistochemical de-

* *References 4–6, 11, 16, 18, 19, 29, 35, 42, 45, 48, 50, 60.*

Table 2. List of the Differential Diagnoses
Nodular pseudoangiomatous stromal hyperplasia[74,77,78]
Nodular fasciitis[79,80]
Post–fine-needle aspiration cytology reactive spindle cell nodule[81]
Leiomyoma[82,83]
Spindle cell lipoma[84]
Benign peripheral nerve sheath tumor[82,85,86]
Angiomyolipoma[87]
Benign fibrohistiocytoma[88]
Solitary fibrous tumor[22,89]
Desmoid-type fibromatosis[90–92]
Inflammatory myofibroblastic tumor[93]
Low-grade myofibroblastic sarcoma[94]
Dermatofibrosarcoma protuberans[95]
Low-grade fibromatosis-like carcinoma[96,97]
Malignant myoepithelioma[98]
Low-grade fibrosarcoma[99,100]
Leiomyosarcoma[82,101]
Low-grade malignant peripheral nerve sheath tumors[102]
Spindle cell liposarcoma[103]
Follicular dendritic cell tumor[104]

tails, helpful to rule out each of the entities described above, have been discussed extensively elsewhere.[1,2,55,77–109]

CONCLUSIONS

Establishing a correct diagnosis of MFB may be challenging, especially when interpreting an unusual variant of this tumor or when one is faced with FNAC or core needle biopsy. The purpose of this review is to assist the pathologist in the recognition of MFB and its more unusual variants by providing their clinicopathologic features as well as pertinent histologic illustrations. The importance of recognizing the diverse morphologic appearances of MFB is emphasized to avoid a misdiagnosis of malignancy. Although histology remains preeminent in the diagnosis of MFB, immunohistochemistry is crucial in some cases.

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