#### Review

## Practical approach to diagnosis of bland-looking spindle cell lesions of the breast

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#### Summarv

The diagnosis of bland-looking spindle cell lesions of the breast is often challenging because there is a close morphological and immunohistochemical overlap among the different entities. The present review will discuss reactive spindle cell nodule/exuberant scar, nodular fasciitis, inflammatory pseudotumor, myofibroblastoma (classic type), lipomatous myofibroblastoma, palisaded myofibroblastoma, benign fibroblastic spindle cell tumor, spindle cell lipoma, fibroma, leiomyoma, solitary fibrous tumor, myxoma, schwannoma/neurofibroma, desmoid-type fibromatosis, dermatofibrosarcoma protuberans, low-grade fibromatosis-like spindle cell carcinoma, inflammatory myofibroblastic tumor and low-grade myofibroblastic sarcoma arising in the breast parenchyma. The pathologist should be aware of each single lesion to achieve a correct diagnosis to ensure patient a correct prognostic information and therapy. Accordingly representative illustrations and morphological/ immunohistochemical diagnostic clues will be provided.

#### Key words

Spindle cell tumors • Breast parenchyma • Differential diagnosis• Diagnostic approach

## Introduction

Bland-looking spindle cell lesions of the breast comprise a heterogeneous group of tumor-like and tumor entities, ranging from reactive to low-grade malignant neoplasms with metastatic potential <sup>1</sup>. (Tab. I). Accordingly, differential diagnosis between the benign spindle cell lesions and the potentially aggressive tumors is mandatory to avoid overdiagnosis and overtreatment. However, this distinction is often challenging in daily practice, especially in needle core biopsies, due to the morphological and immunohistochemical overlap exhibited by the different lesions that often share bland-looking spindle cells with the morphological features of fibroblasts/myofibroblasts, arranged haphazardly or in short fascicles or with focal storiform growth pattern, and set in a variable fibro-myxoid stroma. Pathologists should be aware

#### Tab. I. Bland-looking spindle cell lesions of the breast.

Reactive lesions	
<ul> <li>Reactive Spindle Cell Nodule/Exuberant Scar</li> <li>Nodular Fasciitis</li> <li>Inflammatory Pseudotumor</li> </ul>	
Benign tumors	
Specific to mammary stroma	Not specific to mammary stroma
<ul> <li>Myofibroblastoma, classic-type</li> <li>Myofibroblastoma, lipomatous</li> <li>variant</li> <li>Myofibroblastoma, palisaded</li> <li>variant</li> <li>Benign Fibroblastic Spindle</li> <li>Cell Tumor</li> </ul>	<ul> <li>Leiomyoma</li> <li>Schwannoma/Neurofibroma</li> <li>Spindle cell lipoma</li> <li>Solitary fibrous tumor</li> <li>Myxoma</li> <li>Fibroma</li> </ul>
Low-grade tumors, locally aggressive	
- Desmoid-type fibromatosis - Dermatofibrosarcoma protuberans	
Low-grade tumors with metastatic potential	
<ul> <li>Low-grade fibromatosis-like spindle cell carcinoma</li> <li>Low-grade myofibroblastic sarcoma</li> <li>Inflammatory Myofibroblastic Tumor</li> </ul>	

How to cite this article: Magro G, Salvatorelli L, Puzzo L, et al. Practical approach to diagnosis of bland-looking spindle cell lesions of the breast. Pathologica 2019;111:344-60. https://doi.org/10.32074/1591-951X-31-19.

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of the morphological and immunohistochemical differences between fibroblasts and myofibroblasts when dealing with a spindle cell lesion of the breast. Recognizing a lesion as predominantly fibroblastic or myofibroblastic in nature may help in the diagnostic approach. Fibroblastic lesions are mainly or entirely composed of elongated spindle cells with scant, pale to slightly eosinophilic cytoplasm, elongated nuclei with absent or only inconspicuous nucleoli. Fibroblasts are usually stained with vimentin and CD34, generic mesenchymal markers lacking any specificity of differentiation cell lineage. Focal and weak staining with  $\alpha$ -smooth muscle actin can be seen. Conversely myofibroblasts -modified fibroblasts with the capability to contract- are plumper than fibroblasts, showing more abundant slightly to deeply eosinophilic cytoplasm and ovoid nuclei with evident small nucleoli. Unlike fibroblasts, myofibroblasts exhibit a more diffuse and strong staining for  $\alpha$ -smooth muscle actin; some lesions, like myofibroblastoma, are typically stained with desmin more than with  $\alpha$ -smooth muscle actin. Finally, the pathologist should be aware that the neoplastic cells of the breast carcinoma, as like in other carcinomas, may adopt a spindled morphology raising confusion with benign/low-grade mesenchymal lesions. This phenomenon is related to an epithelial-mesenchymal transition, i.e. a biologic process due to plasticity of the cells, that consists in the progressive loss of epithelial morphological and immunohistochemical features and gain of a mesenchymal cell profile, including the expression of vimentin and a-smooth muscle actin. Low-grade, fibromatosis-like spindle cell carcinoma is a prototypical example of an epithelial-mesenchymal transition <sup>10</sup>.

In our opinion, the tumor-like and tumor spindle cell lesions of the breast are often underrecognized, with

#### Tab. II. Key diagnostic features.

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<b>Reactive Spindle Cell Nodule/Exuberant Scar:</b> circumscribed and, at least focally, infiltrative margins; previous biopsy/FNA; α-smooth muscle actin-positive spindle cells; foamy and hemosiderin-laden macrophages, lymphocytes and foreign body giant cells; fat necrosis
<b>Nodular Fasciitis:</b> circumscribed and, at least focally, infiltrative margins; $\alpha$ -smooth muscle actin-positive spindle cells; fibro-myxoid stroma, at least focally, with tissue culture-like appearance
<b>Inflammatory Pseudotumor</b> : circumscribed and, at least focally, infiltrative margins; α-smooth muscle actin-positive spindle cells closely intermingling with lymphocytes and plasma cells; previous history of local trauma/stimuli; ALK-1 is negative
<b>Myofibroblastoma</b> , <b>Classic-type</b> : circumscribed margins; desmin/CD34/α-smooth muscle actin-positive spindle cells; short intersecting fascicles interrupted by keloid-like collagen fibers
<b>Lipomatous Myofibroblastoma:</b> circumscribed margins; desmin/CD34/α-smooth muscle actin-positive spindle cells with finger-like pseudo-infiltration into an intratumoral lipomatous component
<b>Palisaded/Schwannian Myofibroblastoma:</b> circumscribed margins; desmin/CD34/α-smooth muscle actin-positive spindle cells with formation of Verocay-like bodies; S100 protein is negative
Benign Fibroblastic Spindle Cell Tumor: circumscribed margins; CD34-positive fibroblastic-like spindle cells; short intersecting fascicles; thick keloid-like collagen fibers; variable additional lipomatous component
<b>Spindle Cell Lipoma:</b> circumscribed margins; CD34-positive short spindle cells with bipolar cytoplasmic processes; variably admixed mature lipomatous component; at least focally, myxoid stroma with ropey collagen fibers
Fibroma: circumscribed margins; hypocellular, fibrosclerotic nodule with interspersed CD34-positive fibroblast-like spindle cells
Solitary Fibrous Tumor: circumscribed margins; CD34/STAT6-positive fibroblast-like spindle cells, haphazardly arranged (pattern-less growth pattern); branching vessels, often with perivascular hyalinization
<b>Leiomyoma:</b> circumscribed margins; interlacing fascicles of desmin/ $\alpha$ -smooth muscle actin/h-caldesmon-positive spindle cells with the features of mature smooth muscle cells_
Myxoma: circumscribed margins; vimentin positive spindle to stellate cells embedded in an abundant myxoid stroma; atypical bizarre cells, along with thick keloid-like collagen fibers, can be seen
Schwannoma/Neurofibroma: circumscribed margins; S100-positive spindle cells with formation of Verocay-bodies and alternating Antoni A and Antoni B areas (schwannoma); cells with wavy nuclei set in myxoid stroma with keloid-like collagen fibers (neurofibroma)
<b>Desmoid-type Fibromatosis:</b> finger-like infiltrative margins; $\alpha$ -smooth muscle actin and $\beta$ -catenin-positive fibroblast/myofibroblast-like spindle cells arranged into long intersecting fascicles; the cells are often aligned parallel and are separated by collagenized stroma
<b>Dermatofibrosarcoma Protuberans:</b> circumscribed and, at least focally, infiltrative margins; CD34-positive fibroblast-like spindle cells; diffuse storiform growth pattern; low mitotic activity; finger-like or honeycomb infiltration of the adjacent fibro-fatty tissue
Low-grade, Fibromatosis-like Spindle Cell Carcinoma: finger-like infiltrative margins; p63/cytokeratin-positive spindle cells with the features of fibroblasts/myofibroblasts; at least focally, small cohesive clusters of cytokeratin/p63-positive epithelioid-polygonal cells
<b>Inflammatory Myofibroblastic Tumor:</b> circumscribed and, at least focally, infiltrative margins; α-smooth muscle actin-positive spindle cells admixed with lymphocytes and plasma cells; no association with previous history of local trauma/stimuli; ALK-1 expression in about 40-50% of cases

**Low-grade Myofibroblastic Sarcoma:** circumscribed and, at least focally, infiltrative margins; α-smooth muscle actin-positive myofibroblastic-like cells with mild/moderate nuclear pleomorphism and high mitotic activity (7 to 35 mitoses x 10 HPF); fascicular arrangement

#### Tab. III. Differential diagnoses between benign versus low-grade lesions.

Nodular fasciits versus Desmoid-type Fibromatosis

Shared features: at least focally, infiltrative margins with entrapment of mammary ducts/lobules; α-smooth muscle actin-positive spindle cells in a variable fibro-myxoid stroma

**Distinguishing features:** desmoid-type fibromatosis shows long intersecting fascicles with cells aligned parallel, whereas nodular fasciitis exhibits cells haphazardly arranged or forming short fascicles with focal storiform growth pattern; unlike nodular fasciitis, desmoid-type fibromatosis is usually stained with  $\beta$ -catenin (nuclear staining)

Lipomatous Myofibroblastoma versus Desmoid-type Fibromatosis

Shared features: a-smooth muscle actin-positive spindle cells in a fibrous stroma, with finger-like extension into mature adipose tissue

**Distinguishing features:** desmoid-type fibromatosis exhibits infiltrative margins, whereas lipomatous myofibroblastoma shows pushing borders; adipose tissue is an integral part of the lipomatous myofibroblastoma, whereas adipose tissue in desmoid-type fibromatosis is mammary fat infiltrated by neoplastic cells; lipomatous myofibroblastoma is stained with desmin, CD34 and estrogen/progesterone receptors, whereas desmoid-type fibromatosis is negative to these markers, but positive for  $\beta$ -catenin

Classic-type Myofibroblastoma versus Low-grade Myofibroblastic Sarcoma

Shared features: circumscribed borders,  $\alpha$ -smooth muscle actin-spindle cells arranged in short fascicles with variable fibro-myxoid stroma

**Distinguishing features:** low-grade myofibroblastic sarcoma is more cellular and the spindle cells show, at least focally, moderate nuclear pleomorpshism, nuclear overlapping, as well as high mitotic activity (7 to 35 mitoses x 10 HPF); myofibroblastoma is a tumor with absent to low mitotic activity (up to 2 mitoses x 10 HPF), that variably co-expresses desmin, CD34 and estrogen/progesterone receptors

Desmoid-type Fibromatosis versus Low-grade Fibromatosis-like Spindle Cell Carcinoma

Shared features: infiltrative margins with entrapment of mammary ducts/lobules and fat; α-smooth muscle actin-positive spindle cells set in a fibrous stroma

**Distinguishing features:** desmoid-type fibromatosis shows long intersecting fascicles with cells often aligned parallel, but lacks pancytokeratins/p63-positive spindle to focally epithelioid-polygonal cells arranged in small cohesive clusters

confusion in the distinction between reactive versus neoplastic (benign or low-grade malignant) lesions. Although some difficulties are due the fact that different names are often used to indicate the same entity, it is also true that a single name is applied to biologically different lesions. In addition, we think that potential diagnostic errors are likely to occur because the pathologist: i) is faced with an unfamiliar lesion (myofibroblastoma; low-grade myofibroblastic sarcoma; low-grade fibromatosis-like spindle cell carcinoma); ii) pathologist is not familiar with soft tissue pathology (nodular fasciitis; desmoid-type fibromatosis; solitary fibrous tumor; low-grade myofibroblastic sarcoma); iii) may encounter diagnostic difficulties when dealing with a typical soft tissue lesion/tumor occurring in an unexpected site, such as in the breast (nodular fasciitis, desmoid-type fibromatosis, solitary fibrous tumor, leiomyoma, schwannoma, spindle cell lipoma). The present overview focuses on the morphological and immunohistochemical features helpful to recognize each single entity in the wide spectrum of the bland-looking spindle cell lesions of breast parenchyma (Tab. II). Representative illustrations along with the main diagnostic clues are provided (Tab. III).

## **Reactive lesions**

#### **R**EACTIVE SPINDLE CELL NODULE/EXUBERANT SCAR <sup>11-15</sup>

It should be suspected in presence of a fairly circumscribed nodule, arising after biopsy/FNAC or surgical procedures, composed of  $\alpha$ -smooth muscle actin-positive spindle cells with the features of myofibroblasts, set in a variably fibro-myxoid stroma containing both foamy and hemosiderin-laden macrophages, lymphocytes and foreign body giant cells (Fig. 1A). Fat necrosis and entrapment or displacement of normal mammary glands/ducts are frequent-ly encountered (Fig. 1A,B). The reactive spindle cells may be, at least focally, arranged into short fascicles (Fig. 1C), focally exhibiting a storiform growth pattern. Mitotic activity is low, ranging from 1 to 4 mitoses x 10 high power fields.

#### NODULAR FASCIITIS 16-20

It should be suspected in presence of a nodule with partially circumscribed margins, composed of a proliferation of  $\alpha$ -smooth muscle actin-positive spindle cells with the features of myofibroblasts and brisk mitotic activity; the cells are arranged into short, not well-formed fascicles and focally in whorls or storiform growth pattern (Fig. 2A). The stroma, variably



Fig. 1. Reactive spindle cell nodule/exuberant scar. (A) Fibro-inflammatory tissue with spindle cells; (B) fat necrosis is a diagnostic clue; (C) fibro-sclerotic stroma with interspersed spindle cells, entrapping a mammary duct.

myxoid with microcystic degeneration to fibrous in nature (Fig. 2B) and containing red blood cells and lymphocytes, shows, at least focally, a tissue culture-like morphology (Fig. 2C). Mammary ducts/lobules can be entrapped, especially at the periphery of the lesion (Fig. 2A). Surgical excision is curative with rare local recurrence (< 2% of cases, including lesions incompletely excised).

#### INFLAMMATORY PSEUDOTUMOR 21-27

It should be suspected in the presence of a fairly circumscribed nodule arising in association with local trauma/stimuli; it is composed of  $\alpha$ -smooth muscle actin-positive spindle cells with the features of myofibroblasts, closely intermingling with lymphocytes and plasma cells (Fig. 3A, B); cells are usually arranged in interlacing short bundles (Fig. 3C) or may exhibit swirling/storiform growth pattern; atypical/bizarre mono- or multi-nucleated cells can be, at least focally, encountered (Fig. 3D); defining the boundaries between a reactive (inflammatory pseudotumor) *versus* a true neoplastic process (inflammatory myofibroblastic tumor) still remains to be established. Surgical excision is curative.

## **Benign tumors**

## MYOFIBROBLASTOMA, CLASSIC-TYPE 28 29

It should be suspected in presence of a well-circumscribed nodule (Fig. 4A) composed of a proliferation of desmin/CD34/ $\alpha$ -smooth muscle actin-positive spindle cells with the features of myofibroblasts, arranged into short, haphazardly intersecting fascicles interrupted by thick keloid-like collagen bands (Fig. 4B). Focal storiform or neural-like growth patterns can be seen, including a minor component of neoplastic



**Fig. 2. Nodular fasciitis.** (A) Spindle cell proliferation with fibrous stroma and entrapped mammary ducts at the periphery of the lesion; (B) area with myxo-edematous stroma containing inflammatory cells (tissue culture-like appearance); (C) extravasated erythrocytes can be seen.

cells with epithelioid morphology. Mitotic activity is low (0-2 mitoses x 10 high power field). The stroma is usually fibrous to focally myxoid and may contain islands of mature adipose tissue. Mast cells are variably interspersed among neoplastic cells. Usually no entrapment of mammary ducts/lobules is seen. Surgical excision is curative.

## LIPOMATOUS MYOFIBROBLASTOMA 30-33

It should be suspected in presence of a well-circumscribed fibro-fatty nodule (Fig. 5A), composed of a proliferation of desmin/CD34/ $\alpha$ -smooth muscle actin-positive spindle cells with the features of myofibroblasts that exhibit a finger-like pseudo-infiltration into an intratumoral lipomatous component (Fig. 5B). Although this pattern is reminiscent of desmoid-type fibromatosis or low-grade (fibromatosis-like) spindle cell carcinoma, tumor margins are pushing and not infiltrative (Fig. 5B); areas with the typical features of myofibroblastoma are identified, at least focally (Fig. 5C). Surgical excision is curative.

## PALISADED MYOFIBROBLASTOMA 34-36

It should be suspected in presence of a well-circumscribed nodule, histologically reminiscent of schwannoma (Fig. 6A). It is composed of desmin/CD34/ $\alpha$ smooth muscle actin-positive spindle cells exhibiting a prominent nuclear palisading, with formation of numerous Verocay-like bodies: two compact rows of well aligned nuclei separated by myxoid matrix (Fig. 6A-C). Mitotic activity is low (0-2 mitoses x 10 high power field). As in other myofibroblastoma variants, keloid-like eosinophilic collagen fibers are dispersed throughout the myxoid stroma and between neoplastic cells; areas with the typical features of myofibroblastoma can be seen, at least focally. Surgical excision is curative.

## **B**ENIGN FIBROBLASTIC SPINDLE CELL TUMOR <sup>37-44</sup>

It should be suspected in presence of a well-circumscribed nodule (Fig. 7A) composed of a proliferation of CD34-positive spindle cells with the features of fibro-



Fig. 3. Inflammatory pseudotumor (male patient with local breast trauma). (A) Spindle cells intermingling with inflammatory cells; (B) spindle cells are stained with  $\alpha$ -smooth muscle actin; (C) spindle cells are arranged in a swirling growth pattern; (D) atypical/bizarre cells can be seen.

blasts arranged haphazardly, or in intersecting short fascicles with interspersed keloid-like collagen fibers (Fig. 7B); mitoses are absent to low (0-2 mitoses x 10 high power field). The stroma is collagenized and may contain a prominent lipomatous component (spindle cell lipoma-like morphology). Surgical excision is curative.

#### SPINDLE CELL LIPOMA 45-48

It should be suspected in presence of a circumscribed nodule composed of a proliferation of CD34-positive, short spindle cells, variably admixed with mature adipocytes (Fig. 8A) and set in, at least focally, myxoid stroma containing ropey collagen fibers (Fig. 8B). In the myxoid areas the spindle cells often show long and thin bipolar cytoplasmic processes (Fig. 8B). Mitoses are absent or rare; mast cells are variably scattered throughout the tumor. Surgical excision is curative.

## FIBROMA 43 49

It should be suspected in presence of a well-circumscribed, hypocellular nodule (Fig. 9A) composed of CD34-positive spindle cells with the features of fibroblasts, haphazardly dispersed in a heavily collagenized stroma (Fig. 9B) in which mammary ducts/ lobules can be entrapped; mitotic activity is absent. Surgical excision is curative.

## LEIOMYOMA <sup>50-53</sup>

It should be suspected in presence of a well-circumscribed nodule (Fig. 10A) composed of interlacing fascicles of desmin/ $\alpha$ -smooth muscle actin/h-caldesmon-positive spindle cells with the features of mature



**Fig. 4. Myofibroblastoma, classic-type.** (A) A spindle cell tumor with pushing margins and numerous keloid-like collagen fibers; (B) cells, with eosinophilic cytoplasm and oval nuclei, are arranged in short fascicles with interspersed keloid-like collagen fibers.



**Fig. 5. Lipomatous myofibroblastoma.** (A) Fibrolipomatous tumor with pushing borders; (B) the fibrous component exhibits a finger-like infiltration into the lipomatous component, but the margins are circumscribed; (C) tumor area with the characteristics of classic-type myofibroblastoma: fascicles of spindle cells separated by keloid-like collagen bands.



**Fig. 6. Palisaded/Schwannoma-like Myofibroblastoma.** (A) Tumor with pushing borders, closely reminiscent of Schwannoma; (B) higher magnification showing nuclear palisading with formation of Verocay-like bodies; (C) cells, negative to S100 protein, are stained with  $\alpha$ -smooth muscle actin, revealing their myofibroblastic nature.

smooth muscle cells (deeply eosinophilic cytoplasm with elongated nuclei with blunt ends) (Fig. 10B); absent to low mitotic activity. Surgical excision is curative.

## SOLITARY FIBROUS TUMOR 43 44 54-61

It should be suspected in presence of a well-circumscribed nodule (Fig. 11A) composed of CD34/ STAT6-positive spindle cells with the features of fibroblasts, low mitotic activity (<4 mitoses x 10 HPF), and haphazardly arranged in a fibrous to focally myxoid stroma containing branching vessels, often with perivascular hyalinization (Fig. 11B, C). Surgical excision is curative. Pathologists should always search for morphological features that can be associated with an aggressive clinical course, including >4 mitoses x 10 HPF, nuclear pleomorphism, hypercellularity, necrosis, sarcomatous dedifferentiation.

## Мухома 62-66

It should be suspected in presence of a well-circumscribed nodule (Fig. 12A) composed of vimentin-positive spindle- to stellate-shaped cells dispersed in abundant/exclusive myxoid stroma (Fig. 12B); stromal microcystic spaces simulating lipoblasts are seen. Atypical/bizarre cells, as well as keloid-like collagen fibers, can be occasionally observed (Fig. 12C). Mitotic activity is absent. Surgical excision is curative.

#### SCHWANNOMA/NEUROFIBROMA 51 67-76

It should be suspected in presence of a nodular mass with circumscribed margins, composed of S100-positive spindle cells with wavy nuclei and absent to low mitotic activity; schwannoma shows interlacing fascicles and whorls, as well as palisading nuclei (Verocay bodies) and alternating hypercellular (Antoni A areas) and hypocellular (Antoni B) areas; in neurofibroma the spindle cells are usually haphazardly arranged in a slightly myxoid stroma containing thick collagen fibers. Surgical excision is curative.



Fig. 7. Benign fibroblastic spindle cell tumor. (A) A fibrous tumor with circumscribed borders; (B) spindle cells look like fibroblasts and are arranged in short fascicles set in a collagenized stroma.

## Low-grade tumors, locally aggressive

#### **D**ESMOID-TYPE FIBROMATOSIS<sup>77-82</sup>

It should be suspected in presence of a nodular mass with finger-like infiltrative margins (Fig. 13A), composed of spindle cells with the features of both fibroblasts and myofibroblasts Characteristically the neoplastic cells, often aligned parallel, are arranged in long and sweeping fascicles set in a prominent fibrous to focally myxoid stroma (Fig. 13B,C). Mitoses are rare. These cells are variably stained with  $\alpha$ -smooth muscle actin and  $\beta$ -catenin (nuclear staining in about 80% of cases) (Fig. 13C). Desmoid-type fibromatosis is a locally aggressive tumor that can recur locally but with no metastatic potential.

#### DERMATOFIBROSARCOMA PROTUBERANS 83-87

It should be suspected in presence of a nodular mass with relatively circumscribed margins, composed of CD34-positive spindle cells with the fea-

tures of fibroblasts, low mitotic activity, and diffusely arranged in a storiform growth pattern with finger-like or honeycomb infiltration of the adjacent fibro-fatty tissue (Fig. 14 A-C). Radical excision is curative. Local recurrence is usually due to incomplete surgical excision.

# Low-grade tumors with metastatic potential

#### LOW-GRADE FIBROMATOSIS-LIKE SPINDLE CELL CARCINOMA 88-89

It should be suspected in presence of a nodular mass with finger-like infiltrative margins (Fig. 15A), composed of p63/cytokeratin-positive spindle cells (Fig. 15B) and low mitotic activity; variable co-expression of  $\alpha$ -smooth muscle actin can be seen. The identification, at least focally, of epithelioid-polygonal cells arranged in small cohesive clusters (Fig. 15C), better highlighted by immunohistochemistry (Fig. 15D) is the



Fig. 8. Spindle cell lipoma. (A) A fatty-tumor with interspersed fibro-myxoid areas; (B) higher magnification: myxoid area showing spindle cells with long cytoplasmic bipolar processes and ropey collagen fibers.



**Fig. 9. Fibroma**. (A) A fibrous hypocellular tumor with circumscribed margins; (B) higher magnification showing fibroblast-like spindle cells set in a collagenized stroma.



**Fig. 10. Leiomyoma.** (A) Spindle cell tumor with circumscribed borders and fascicular growth pattern; (B) higher magnification showing smooth muscle cells with deep eosinophilic cytoplasm.



**Fig. 11. Solitary fibrous tumor.** (A) Spindle cell tumor with pushing margins; (B) neoplastic cells are set in a fibrous stroma containing branching blood vessels with perivascular fibrosis; (C) neoplastic cells show diffuse nuclear staining with STAT-6.



**Fig. 12. Myxoma.** (A) A myxoid tumor with circumscribed margins; (B) higher magnification showing spindle and stellate cells embedded in abundant myxoid stroma; stromal microcystic spaces look like univacuolated lipoblasts; (C) neoplastic cells may exhibit nuclear atypia (bizarre cells) and the myxoid stroma may contain keloid-like collagen fibers.

main diagnostic clue for this type of carcinoma. A minority of squamous nests and/or small-sized neoplastic glands can be encountered. Estrogen/progesterone receptors and HER2 are negative (triple-negative carcinoma). This carcinoma can recur locally, with low metastatic potential (lymph node or distant metastases). Radical excision is curative in most cases.

#### INFLAMMATORY MYOFIBROBLASTIC TUMOR 90-94

It should be suspected in presence of a nodular mass with relatively circumscribed margins, with morphological features similar to inflammatory pseudotumor, arising without apparent correlation with local trauma/ stimuli; ALK-1 expression favors this diagnosis. Surgical excision is curative with local recurrence documented in about 15-20% of cases. Rarely distant metastases have been reported.

## LOW-GRADE MYOFIBROBLASTIC SARCOMA 95-98

It should be suspected in presence of a nodular mass with relatively circumscribed margins, composed of a proliferation of mitotically active (from 7 to 35 mitoses x 10 HPF) spindle cells with the features of myofibroblasts, showing, at least focally, moderate nuclear pleomorphism, fascicular arrangement and variable staining for  $\alpha$ -smooth muscle actin. This tumor, which can recur locally, has metastatic potential.

#### **CONFLICT OF INTEREST STATEMENT**

None declared.



**Fig. 13. Desmoid-type Fibromatosis.** (A) Fibrous proliferation with infiltrative margins; (B) bland-looking spindle cells entrap pre-existing mammary ducts; (C) higher magnification showing spindle cells aligned parallel and separated by a fibrous stroma. Neoplastic cells show nuclear expression of  $\beta$ -catenin (insert).



Fig. 14. Dermatofibrosarcoma protuberans. (A) Spindle cell tumor surrounding pre-existing duct/lobular units; (B) the neoplastic cells diffusely infiltrate adipose tissue; (C) neoplastic cells are diffusely stained with CD34.



**Fig. 15. Low-grade fibromatosis-like spindle cell carcinoma.** (A) Low-magnification showing a fibrous tumor with finger-like infiltrative margins; (B) bland-looking spindle cells are set in a fibrous stroma and exhibit a fascicular arrangement; (C) some tumor areas show single or small groups of round to epithelioid cells scattered throughout the fibrous stroma; (D) these neoplastic cells show nuclear expression of p63.



**Fig. 16.** Low-grade myofibroblastic sarcoma. (A) Low-magnification showing a hypercellular tumor with pushing borders; (B) the neoplastic cells, with the morphological features of myofibroblasts, are arranged in short intersecting fascicles; (C) neoplastic cells are diffusely stained with  $\alpha$ -smooth muscle actin.

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Received: October 24, 2019 - Accepted: October 28, 2019