Annales de pathologie (2015) 35, 15—31

Disponible en ligne sur ScienceDirect www.sciencedirect.com

Elsevier Masson France EM|consulte www.em-consulte.com

REVIEW

# Mesenchymal tumors and tumor-like lesions of the breast: A contemporary approach review

## Tumeurs et lésions mésenchymateuses du sein : revue de la littérature

**Simona Stolnicu**[a], **Cosmin Moldovan**[b], **Cristian Podoleanu**[c,*], **Rares Georgescu**[d]

[a] *Department of Pathology, University of Medicine, Tirgu Mures, Romania*
[b] *Department of Histology, University of Medicine, Tirgu Mures, Romania*
[c] *Department of Cardiology, University of Medicine, Tirgu Mures, Romania*
[d] *Department of Surgery, University of Medicine, Tirgu Mures, Romania*

Accepted for publication on 2 October 2014
Available online 20 December 2014

**KEYWORDS**
Breast;
Mammary mesenchymal tumors;
Tumor-like lesions;
Pseudotumors;
Malignant phyllodes tumors;
Sarcomas

**Summary** The classification of the breast tumors has been revised and recently published in 2012 in the WHO blue book. Contrary to the epithelial tumors in the breast, mesenchymal tumors are rare and the classification for benign and malignant tumors is based on the same criteria in both categories, since no other specific diagnostic criteria, which would have an impact on prognosis, exist to date. The present review deals with minor changes mirroring the recent developments in the benign mesenchymal tumors (new additions are nodular fasciitis and atypical vascular lesions, while the haemangiopericytoma is removed) focusing especially on criteria to diagnose sarcomas, which represent a wide spectrum including very difficult lesions. The majority of sarcomas of the breast arise as a component of a malignant phyllodes tumor, while the pure forms are very rare. When a pure primary sarcoma of the breast is diagnosed, pathologists are encouraged to categorize the lesion according to the type of differentiation and to provide to the clinicians all the important prognostic parameters for the best treatment choice.


**MOTS CLÉS**
Sein ;
Glande mammaire ;

**Résumé** La classification des tumeurs du sein a été révisée et publiée en 2012 par l'OMS. Contrairement aux tumeurs épithéliales du sein, les tumeurs mésenchymateuses sont rares ; la classification des tumeurs bénignes et malignes est basée sur les mêmes critères dans

* Corresponding author.
*E-mail address:* podoleanu@me.com (C. Podoleanu).

http://dx.doi.org/10.1016/j.annpat.2014.10.001

Tumeurs mésenchymateuses du sein ;
Lésions mammaires mimant des tumeurs ;
Pseudotumeur ;
Sarcomes ;
Sarcomes phyllodes

ces deux catégories, car aucun autre critère de diagnostic spécifique, qui aurait un impact sur le pronostic, n'existe à ce jour. Cette revue de la littérature traite des modifications mineures reflétant les développements récents pour les tumeurs mésenchymateuses bénignes (nouveaux ajouts : fasciite nodulaire et lésions vasculaires atypiques, tandis que le diagnostic d'hémangiopéricytome est retiré de la classification). Un accent particulier est mis sur les critères permettant de diagnostiquer les sarcomes qui représentent un large spectre de lésions parfois très difficiles à classer. La majorité des sarcomes du sein se développe à partir d'une tumeur maligne phyllode, alors que les formes pures (non phyllodes) sont très rares. Quand un sarcome primaire pur du sein est diagnostiqué, les pathologistes doivent classer la lésion en fonction du type de différenciation et fournir aux cliniciens tous les paramètres importants pour le pronostic qui permettront d'adapter au mieux le traitement.


## Introduction

Over the last decade a relatively small number of papers have been published on mesenchymal tumors and tumor-like conditions compared to the large number of papers dedicated to the epithelial lesions of the breast (breast carcinoma and precursor lesions). The recently published WHO blue book focused on minor changes mirroring the recent developments in the mesenchymal tumors, concerning especially the molecular and genetic findings [1].

The mesenchymal lesions of the breast can be benign or malignant and have to be differentiated from tumor-like lesions. Benign tumors are rare and few of them are difficult to diagnose on pathologic examination. However, sarcomas of the breast are very problematic tumors. Firstly, sarcomas are very rare (apart from angiosarcoma), representing less than 1% of all malignancies of the breast [2]. Secondly, they represent a wide spectrum of lesions and have been described only in case reports or small series, in which some of them have been nominated as stromal sarcoma or differently. This is the reason why it is very difficult to determine the accurate frequency of these lesions. In other series, angiosarcomas were excluded or malignant phyllodes tumors were included together with benign or borderline lesions. However, the majority of sarcomas of the breast arise as a component of a malignant phyllodes tumor, while the pure forms are very rare. Also, some metaplastic carcinomas have been mistaken for sarcomas before immunohistochemistry was widely used. Most of the sarcomas of the breast occur in adults, with the exception of the rhabdomyosarcoma, which tend to be seen in children (the embryonic and alveolar type) and are rapidly growing masses with non-specific radiological findings. Since the incidence of local recurrence is high, total mastectomy should be recommended in most sarcomas of the breast. On the other hand, axillary lymph node metastases are extremely uncommon at the time of primary therapy, so sentinel lymph node and axillary lymph node dissection are not routinely indicated [3,4]. The most important prognostic parameters are the number of mitoses, the degree of nuclear atypia and the extent of necrosis. Contemporary multimodal approaches including radiation and chemotherapy may improve the outcome and reduce the frequency of local recurrences.

The classification of sarcomas is based on the same criteria employed for benign mesenchymal lesions, since no other specific diagnostic criteria, which would have an impact on prognosis, exist.

## Benign mesenchymal tumors

### Nodular fasciitis

According to the latest and previous editions of the WHO book, the group of mesenchymal lesions also includes the nodular fasciitis [5,6]. Nodular fasciitis is a monoclonal proliferation of fibroblasts and myofibroblasts, considered now a distinct tumor that needs to be differentiated from other benign, malignant tumor or tumor-like lesions with spindle cells that may arise in the breast parenchyma or subcutis [7]. The term of pseudosarcomatous fasciitis, a synonym that has been previously used for this lesion, has to be avoided as being confusing. Genetic analysis revealed that nodular fasciitis is associated with MYH9-USP6 gene fusion [8]. This is a very rare lesion that mostly occurs in adults. Due to its rapid growth, it may be clinically associated with pain. Macroscopically, the tumor is well circumscribed (but lacks a capsule) and has a grey color. Microscopically, spindle cells with eosinophilic cytoplasm and bland nuclei are arranged in fascicles and are surrounded by a myxoid stroma, which contains inflammatory cells and thin-walled vessels. Immunohistochemically, the cells are positive for actin, while CD34, S100 protein and keratins are negative. Most of these lesions may regress spontaneously if unexcised.

### Benign vascular lesions

Hemangioma, atypical vascular lesions and angiomatosis represent benign vascular lesions. The hemangiopericytoma does not belong to this group of tumors anymore since this is a very rare lesion in the breast despite the possible relationship with myofibroblastoma and spindle cell lipoma [1,9].

#### Hemangioma

Hemangioma is a benign mesenchymal tumor appearing in the breast both in women and in men at any age (including very young patients) with a mean age of onset of 48 years. Although usually non-palpable, on gross examination the lesion is very well delineated, with an average diameter of 0.5—2 cm, a reddish-brown color and a spongy consistency. However, we have encountered larger hemangiomas in routine practice, especially of cavernous type (Fig. 1). Microscopically, it consists of a proliferation of numerous interconnected blood vessels lined by endothelial cells surrounded by a scant fibrous stroma. The lumen of the vessels