

## BENIGN MESENCHYMAL BREAST TUMORS

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### BENİGN MEZENŐİMAL MEME TÖMÖRLERİ

#### ÖZET

Memede görölen neoplazmların büyük çođunluđu memedeki epitel dokusundan köken almaktadır. Klinikte memedeki mezenőimal dokuların hem benign hem de malign neoplazmları oldukça nadir olarak karřımıza çıkmaktadır. Memenin malign mezenőimal tümörleri uluslararası rehberlerde belirlendiđi gibi tedavi edilmektedir. Buna karřın, benign mezenőimal tümörler nadir olarak göröldüklerinden tanı, tedavi ve takipleri konusunda detaylı bilgi ve öneri mevcut deđildir. Benign mezenőimal tümörler klinikte saptandıklarında malign tümörlere olan benzerlikleri nedeniyle sorun oluşturmaktadır. Bu gruptaki tümörlerin klinik ve radyolojik özelliklerinin iyi bilinmesi malign tümörlerden ayırıcı tanısında yardımcı olacaktır.

Anahtar sözcükler: meme, mezenőimal, benign, tümör

### ABSTRACT

The majority of the breast neoplasms originate from the epithelial tissue in the breast. Both benign and malignant neoplasms of the mesenchymal tissue in the breast are rarely encountered in clinical practice. Malignant mesenchymal tumors of the breast tissue are treated according to the international guidelines. In contrast, since benign mesenchymal tumors are rarely diagnosed, detailed knowledge and recommendations about their diagnosis, treatment and follow-up are not present. Benign mesenchymal tumors, when encountered in clinical practice, cause a problem due to their resemblance to malignant tumors. Having a better knowledge of clinical and radiological properties of this group of tumors will help to distinguish them from malignant tumors.

Key words: breast, mesenchymal, benign, tumor

### Introduction

Mesenchymal tissue of the breast contains various cell groups and clinically, many benign and malignant tumors originating from the mesenchymal tissue are detected. There is not much debate over the diagnosis and treatment protocols of malignant mesenchymal tumors. Since benign mesenchymal tumors are very rarely diagnosed, a quantity of detailed clinical data is not available. In addition, since studies about these tumors do not contain many patients, changes in the diagnostic and treatment principles are not frequently encountered. The frequency of benign mesenchymal tumors increased as the use of mammography increased. The most important problem with these tumors is clinical and radiological misdiagnosis as malignant lesions. At the same time, the relation between these rarely encountered lesions and cancer should be known. Even though the diagnosis with needle biopsies is benign in these tumors with a large morphologic spectrum, typing could be difficult. Radiological investigations should be used together in most cases. Some of these tumors could be followed without surgery whereas others require surgical treatment. In addition, there are locally aggressive tumors with a risk of recurrence. Clinicians should be aware of these lesions to explain their importance to the patients, not to under or over treat the

patients, and to avoid unnecessarily frequent follow-ups. For these reasons, we aimed to report the updated data regarding benign mesenchymal tumors in this review.

### Myofibroblastoma

Myofibroblastoma, included in the benign spindle cell tumors of breast stroma, is an extraordinary tumor due to its cell content. In addition to basically having stromal cells, it includes fibromyofibroblastic cells and cells with myoid differentiation (1). Usually, it presents in patients at an advanced age (50-90 years) as unilateral, well-circumscribed mass. Size of the tumors changes between 1-10 cm and affects both gender equally. The reported incidence of these tumors increased as the use of mammography increased. Due to the presence of histologically extraordinary parts, it is a hardly diagnosed tumor. Especially when examining fine needle and core needle biopsy specimens, wide morphological spectrum of this tumor should be kept in mind. Microscopically, in a fibrous stroma, spindle cell proliferation with a few mitoses is prominent (2). These tumors are stained strongly with desmin and smooth muscle actin with immunohistochemistry. Total excision of myofibroblastoma is sufficient for treatment.

Besides myofibroblastomas, there are very rarely reported inflammatory myofibroblastic tumors. In this group of tumors, lymphocyte and histiocyte infiltration is seen in addition to above-mentioned histological findings. These lesions resemble breast carcinoma more both clinically and radiologically. Inflammatory myofibroblastic tumors tend to be bilateral and recur even after total excision (3).

### **Solitary fibrous tumor**

Solitary fibrous tumor is the new nomenclature for the previously called hemangiopericytoma and rarely diagnosed benign mesenchymal tumors in the breast. Size of these tumors can be between 1 and 19 cm and macroscopically, they are whitish-gray with a firm cut surface (4). Microscopically, they are composed of oval and spindle cells surrounding the breast ducts. Branching vasculature can be seen in the entire tumor. Myofibroblastoma should be remembered first in the differential diagnosis. While hyper and hypocellular areas are seen together microscopically in solitary fibrous tumors, there are sharp boundaries between these areas in myofibroblastoma. Although both of these tumors are stained with CD34 immunohistochemically, solitary fibrous tumor is not stained with myogenic markers (4).

### **Fibromatosis**

Breast fibromatosis, also known as desmoid tumor, compose 0.02% of all breast tumors (5). The most frequently encountered region for fibromatosis is the intraabdominal region. Its incidence in the breast is low and frequently it is diagnosed in the fourth decade. Fibromatosis, basically, occurs as a result of regional proliferation of fibroblasts. Physical examination and mammography findings resemble scirrhous breast carcinoma (6). Previous surgical interventions to the breast and breast prosthesis may increase the risk of fibromatosis (5). Microscopically, fascicles of oval or spindle shape fibroblasts are seen in a collagen matrix. Vimentin and beta-katenin positivity with immunohistochemistry points to the myofibroblastic origin of the tumor. Magnetic resonance imaging may be helpful in the radiological differentiation of the lesion from malignancy (7). Fibromatosis is a locally aggressive tumor and risk of recurrence is high. The tumor should be excised with negative margins for treatment. In a sampling of 32 patients from Memorial Sloan Kettering Cancer Center, the recurrence rate was 29%. Younger age, positive or close margins, and larger tumor size were found as parameters increasing recurrence rate (8). Studies evaluating the role of radiotherapy are still continuing (9).

### **Hemangioma**

Hemangiomas are benign vascular tumors of the breast and they can be located in the breast parenchyma as well as in the skin and subcutaneous tissue of the breast. The rate of hemangiomas in the mastectomy specimens performed for breast cancer was reported as 1.2% (10). Hemangiomas clinically present as painless, well-circumscribed masses. They were reported in all age groups (11). In mammography and ultrasonography, they are detected as oval or lobular shaped, well circumscribed or microlobulated

masses. Their location close to the surface supports hemangioma diagnosis (12).

Hemangiomas have various subtypes. Cavernous hemangiomas, composed of dilated vessels surrounded by endothelial cells, are the most frequently diagnosed (11). Venous hemangiomas, capillary hemangiomas, perilobular hemangiomas are highly rare subtypes. Fine needle aspiration biopsy shows that the lesion does not contain either malignant or pre-malignant areas and hemangiomas can be diagnosed easily. Excision of the lesion is not always necessary; however, proving that the lesion is not an angiosarcoma is important (13). In a Canadian study, hormone replacement therapy was cited as the reason for increasing the size of the hemangiomas (14). In addition, atypical vascular lesions in breast skin and parenchyma were reported in patients receiving radiotherapy after breast conserving surgery. "Atypical vascular lesions" and "intravascular papillary endothelial hyperplasia" that is associated with thrombus formation in breast vessels, developing 3-5 years after radiotherapy are other vascular breast lesions carrying clinically and histologically benign characteristics (15,16).

### **Angiomatosis**

Angiomatosis, also known as diffuse hemangioma, is a benign vascular lesion usually encountered in the extremities of individuals with cardiovascular diseases and smoking habit. Breast angiomatosis are rarely reported (17). It can be diagnosed in all age groups and be congenital (18). Clinically, it presents as erythematous plaques and superficial ulcerations in the breast skin and masses located under these lesions. Very large lesions result in diffuse enlargement in the breast. Histologically, a widely dispersed sinusoidal network composed of anastomosing small and large vessels is detected in the breast parenchyma. These lesions tend to recur and histologically to differentiate them from low-grade angiosarcomas may be difficult. For this reason, they should be excised macroscopically with negative surgical margins (19). In addition, very large lesions may necessitate mastectomy. Morrow et al. reported that, although the lesion does not contain hormone receptors, it might grow during pregnancy (19). There is no evidence to prove a relation between angiomatosis and breast cancer or breast cancer risk (18).

### **Pseudoangiomatous stromal hyperplasia**

It is one of the rare proliferative mesenchymal diseases of the breast. It is a lesion where dense collagen proliferation forms slit like spaces in breast parenchyma. It is named as such due to the similarity of these spaces to vascular areas (20). It is mostly seen in the fourth decade. Most commonly, it is diagnosed after breast biopsies performed for other reasons. Rarely, it presents as painless, firm, mobile, palpable mass. Nodular type clinically resembles fibroadenoma or breast hamartoma and presents as a diffuse lesion filling the entire breast (21,22). It resembles fibroadenoma in mammography and ultrasonography and is classified as BIRADS 3 (probably benign) lesion (23). Fine needle aspiration biopsy shows benign properties of the lesion, but reaching a final diagnosis is

difficult. Wieman et al. reported sensitivity of core needle biopsy for pseudoangiomatous stromal hyperplasia as 83% (24). Nodular lesions should not be removed surgically. Patients should be followed regularly. Radiologically BIRADS 4 or 5 lesions and lesions enlarging during follow-up should be totally excised.

### Hamartoma

Hamartoma is a rarely diagnosed benign breast lesion. Clinically, it presents as a relatively large, round, mobile and painless mass. Some of them are incidentally diagnosed in mammography. It is frequently seen in perimenopausal women. Benign breast nodules contain various amounts of adipose and fibrous tissue. There is a pseudo-capsule resulting from its pressure on surrounding breast tissue. Radiologically, they are detected as well-circumscribed, solid, oval lesions without micocalcifications. In ultrasonography, they are seen as hyperechoic lesions without an acoustic shadow (25). Epithelial and mesenchymal parts are seen in cytology. For this reason, it is difficult to diagnose with fine needle aspiration biopsy. Tse et al., in their study evaluating fine needle aspiration biopsies in 25 patients with the diagnosis of hamartoma verified after excision, reported that there were no specific histological diagnostic criteria for fine needle and core needle biopsies and these methods were not reliable enough (26). Sumana et al. thought that lipid cells were frequently seen in fine needle biopsies and hamartomas were misdiagnosed as lipomas (27). In contrast to these, Gomez-Aracil et al. accepted fine needle aspiration biopsy as a reliable technique in their 9 patient studies (28).

Until today, only 14 invasive ductal carcinoma cases developed from hamartoma have been reported in the literature. For this reason, in addition to the difficulty in diagnosis, hamartomas should to be surgically removed (29).

### Pseudoaneurysm

Pseudoaneurysm formation in the breast is frequently observed after a trauma and is accepted as a complication of diagnostic percutaneous biopsies (30). It is a lesion resulting from extravasation following a tear in one of the parenchymal mammary arteries and hematoma formation in the potential space around the artery. Risk is higher in elderly with atherosclerosis and in individuals using anti-coagulants. Almost all patients with very rarely reported spontaneous pseudoaneurysm have hypertension (31). They can be easily diagnosed by showing the current between the space and the vessel in Doppler ultrasonography. In previously reported pseudoaneurysm cases following percutaneous biopsy, usually, large biopsy needles were used (32).

If the lesion involves one of the major arteries, pseudoaneurysm may lead to macroscopic hemorrhage. In addition, a growing pseudoaneurysm results in ischemia due to pressure on the surrounding tissues and pain after ischemia. Growing pseudoaneurysm also carries a risk for infections.

For treatment, external compression or endovascular embolization can be performed under ultrasonographic guidance. If these interventions are not successful, the lesion is surgically excised ligating the artery (33).

### Hemangioendothelioma

Hemangioendothelioma is a very rarely diagnosed primary breast tumor. Microscopically, it is composed of round shaped epithelioid cells with large nuclei (34). Hemangioendothelioma can be misdiagnosed as carcinoma due to its epithelioid morphology and immunohistochemical staining with pan-cytokeratins. In addition, hemangioendothelioma can be related to breast prosthesis (35).

### Granular cell tumor

Granular cell tumors are very rare, benign mesenchymal tumors originating from Schwann cells in the peripheral nerves. Most commonly, they are located in the head and neck region and oral cavity in the body. Granular cell tumors located in the breast form 5-8% of all granular cell tumors (36). It is most commonly diagnosed in premenopausal women and encountered more in the black race compared to the white race (37). They present as very firm masses with skin involvement clinically and radiologically as irregular masses. They resemble breast cancer with these characteristics (37). In contrast to breast cancer, they are more frequently located in the upper inner quadrant. In differential diagnosis using radiology, magnetic resonance imaging is thought to be superior (38,39). Fine needle aspiration biopsy proves that the lesion is not malignant, but the lesion is usually removed surgically due to its resemblance to breast cancer. Its macroscopic cut surface is gray-white in color. Microscopically, cells having a very coarse, granular cytoplasm (granular cells) infiltrate the collagen matrix (40). These granules in the cells were shown to originate from lysosomes in electron microscopy. Final diagnosis is made with immunohistochemical staining. Granular cell tumors stain with PAS, CD68, S100, and NSE and do not stain with cytokeratins. Since granular cell tumors are benign, wide local excision is adequate for the treatment.

### Lipoma

Lipomas are rarely diagnosed, small, benign lipomatous neoplasms. They are frequently seen in perimenopausal women. In breast examination, they are felt as well-circumscribed, soft masses. Morphologically, they are lesions resembling fat tissue, well circumscribed, with a thin capsule. They cannot be detected in mammography and ultrasonography. The diagnostic value of fine needle aspiration biopsy is low. In Lanng's prospective study including 108 patients clinically diagnosed with breast lipoma, mammography detected only 3% of the lesions whereas ultrasonography detected 21%. In 74% of the lesions only lipid cells were seen in fine needle aspiration biopsy. Only in 9 patients lipoma was diagnosed with clinical and radiological evaluation and fine needle aspiration biopsy (triple test). Clinical diagnosis was correct in 75% (41). Verifying the lesion in mammography

or ultrasonography is not a rule for lesions clinically resembling lipoma. If there are no other radiologically suspicious lesions, lipid cells are seen in fine needle aspiration biopsy or core needle biopsy supports the diagnosis, there is no need to remove the lesion. Although they are mostly small lesions, giant lipomas filling the entire breast were reported (42). Degenerative changes such as regional lipid necrosis, calcifications and hyalinization can be encountered in lipomas.

Various subtypes of lipoma can be diagnosed in the breast. Adenolipoma is a benign fat tissue tumor containing lobular epithelium. Angiolipoma is a subcutaneous lesion containing mostly thrombosed, small capillary vessels. Chondrolipoma contains hyaline type cartilage plaques disseminating into a fat nodule (43).

In Özkayalar et al.'s study evaluating mesenchymal breast tumors from our country, lipoma (63%) was the most common benign mesenchymal breast tumor. In this study, the mean size of the lipomas was 3.5 cm and all of them were totally removed (44).

## Leiomyoma

Leiomyoma is a benign tumor of smooth muscles. It is most commonly diagnosed in the uterus, small intestine, and esophagus. It is very rarely reported in the breast. Since most of the breast lesions originate from smooth muscles in the nipple, these tumors are located in the subareolar region (45). Leiomyomas located in the parenchyma are much rarer and they are thought to originate from smooth muscles of the vessels (46). They present with nipple discharge and continuous pain, tenderness, and engorgement in the nipple. Parenchymal lesions can be felt as well-circumscribed nodular masses. They are detected as well-circumscribed round lesions in mammography (47). Lesion should be totally removed for treatment. The nipple and areola should also be removed in some cases (48).

Piloleiomyomas are benign smooth muscle tumors originating from erector pilori muscles of the skin. These are painful lesions. In addition, piloleiomyoma cases occurring over the breast skin have also been reported (49).

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