

# MALIGNANT PHYLLODES TUMOR OF THE BREAST WITH OSTEOSARCOMATOUS DIFFERENTIATION

## MEMENİN OSTEOSARKOMATÖZ DİFERANSİYASYONLU MALİGN FİLLODES TÜMÖRÜ

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This case was presented as a poster at the 23<sup>th</sup> European Pathology Congress, 2011.

### ABSTRACT

Phyllodes tumors are rare biphasic tumors of the breast. The stromal component may show homologous and heterologous sarcomatous elements, including osteosarcomatous differentiation. Here we report a 63 year-old lady who presented with a right breast lump diagnosed as a malignant phyllodes tumor showing predominantly osteosarcomatous differentiation with clinicopathological features.

**Key words:** Phyllodes, tumor, breast, osteosarcoma

### ÖZET

Fillodes tümör memenin nadir bifazik tümörüdür. Stromal komponentte, osteosarkomatöz diferansiyasyonu da içeren, homolog ve heterolog sarkomatöz elemanlar görülebilir. Biz burada, 63 yaşında, sağ memede kitle ile başvuran, osteosarkomatöz diferansiyasyon gösteren bir olguyu klinikopatolojik özellikleri ile birlikte sunduk.

**Anahtar sözcükler:** Fillodes, tümör, meme, osteosarkom

Phyllodes tumors are rare fibroepithelial lesions that account for under 1% of all breast neoplasms (1, 2). Based on the histological characteristics of the tumor, including its surgical margin, stromal cellularity, stromal overgrowth, tumor necrosis, cellular atypia and the number of mitoses per high power field (HPF), it is classified into benign, borderline and malignant categories (3). Histologically malignant phyllodes tumors may show considerable morphological heterogeneity such as liposarcomatous, fibrosarcomatous, rhabdomyosarcomatous, chondrosarcomatous or osteosarcomatous differentiation (4). Osteosarcomatous differentiation of a malignant phyllodes tumor of the breast is extremely rare. There are no predisposing factors and the etiology of a phyllodes tumor is unknown (5). Although there is no proven benefit of either radiotherapy or chemotherapy, radiotherapy can be used (6).

### Case Report

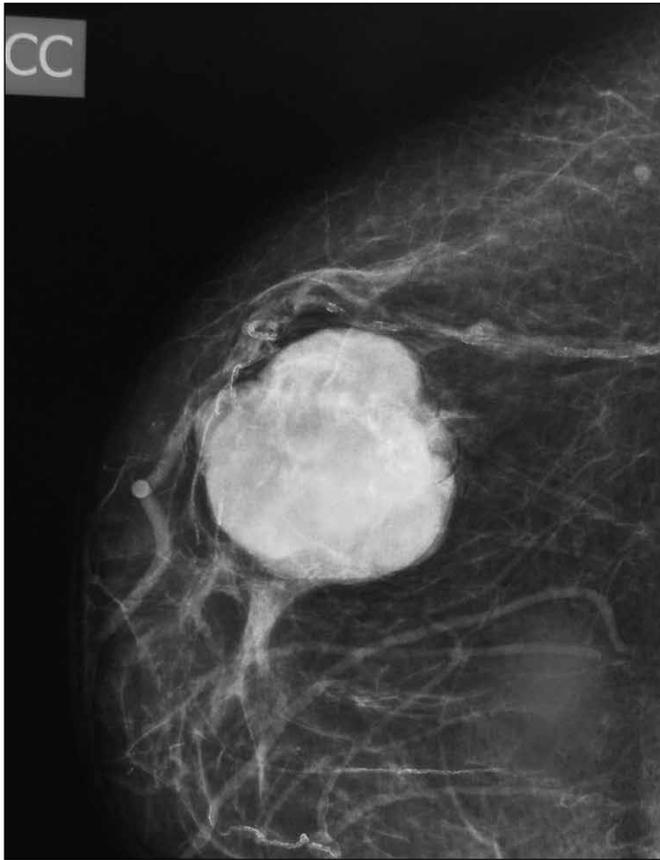
A 63 year-old postmenopausal woman was admitted with a painless mass which had enlarged within two months in her right breast. She had no past history of malignancy and no history of prior irradiation to the breast or chest region. Physical examination indicated a mobile mass located in the upper outer and mid-

dle quadrants of the right breast. The axillary lymph nodes were not palpable. Mammographically, the tumor was an unilateral, well-defined mass with a smooth lobulated border (Figure 1). A quadranectionomy was performed without axillary dissection.

The specimen handled at the pathology laboratory was 14x9x6 cm in size and 245 gr in weight. Series sections of the specimen showed a well-circumscribed firm to hard solid focally cystic tumor mass measuring 7 cm, with a variegated grayish white appearance (Figure 2). The surgical margins of the resection were free of the tumor.

Microscopically, multiple hematoxylin and eosin-stained slides of the tumor revealed a biphasic tumor with benign epithelial and malignant mesenchymal, sarcomatous components.

A benign epithelial component appeared only sparsely as compressed peripheral cleft-like benign epithelial structures or entrapped abortive round ducts in the tumoral stroma (Figure 3, 4). A hypercellular stromal component was predominant with a stromal overgrowth, mostly comprising osteosarcomatous differentiation with numerous osteoclast-like multinucleated giant cells and osteoblasts surrounding osteoid matrix (Figure 5). Furthermore, a fi-



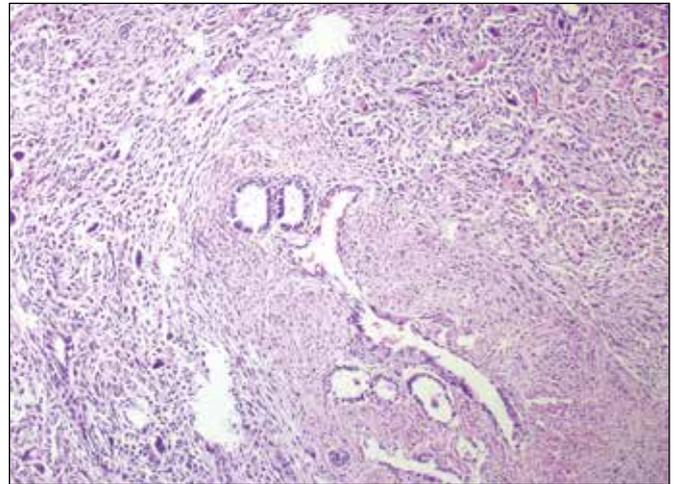
**Figure 1.** The mammography shows a mass well-defined mass with a smooth, lobulated border (Figure 1).



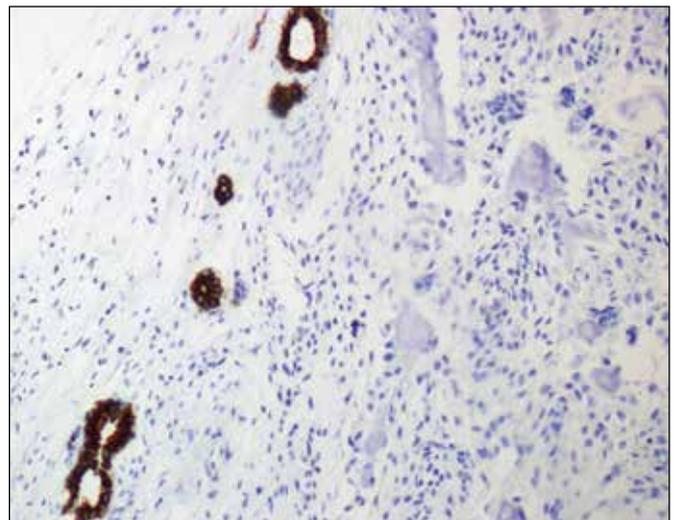
**Figure 2.** On gross examination a solid, greyish white mass with cystic areas is seen.

broblastic spindle cell component and telangiectatic areas accompanied the osteosarcomatous section.

With our research patient, no necrosis was observed, mitotic activity ranged from 6 to 8 per 10 HPF, benign ductal epithelial cells were positive for AE1/AE3, and an overwhelming majority of the sarcomatous cells were positive for vimentin, thus confirming the



**Figure 3.** Benign appearing ductal epithelial component and osteoclast-type giant cells are noted within sarcomatoid stroma (HEX20).

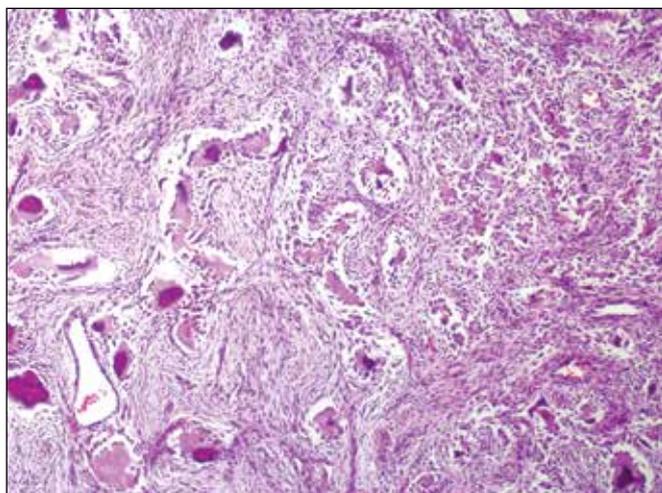


**Figure 4.** Pancytokeratin positivity in abortive ductal epithelial component (X40).

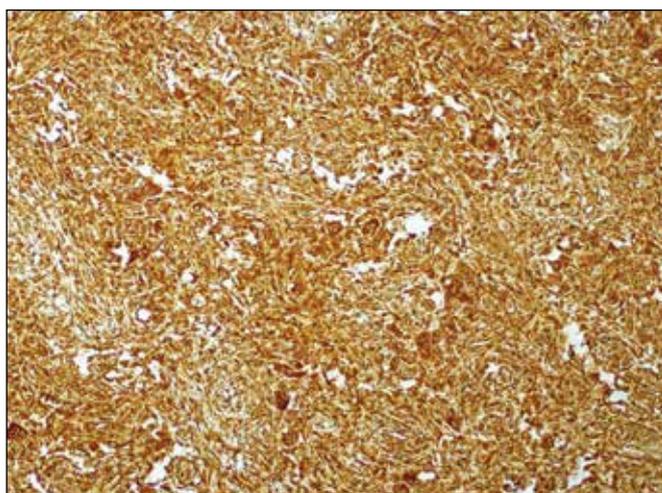
biphasic nature of the neoplasm (Figure 6). Neither cell type expressed desmin, smooth muscle actin, S100, estrogen or progesterone receptors. Based on morphologic and immunohistochemical insignnia, the case was diagnosed as a 'malignant phyllodes tumor of the breast with osteosarcomatous differentiation'.

**Treatment:** As there were no evidence of the lymph node metastasis or a systemic spread (MRI and scintigraphic screening with 99m-Tc methylene diphosphonate), following total surgical excision of the tumor, close follow-up was recommended at the tumor board.

**Outcome:** After ten months following the initial surgery, the patient attended the hospital with a suspicious mass at the surgical incisional site. Fine needle aspiration and frozen section revealed a recurrent malignancy, therefore, simple mastectomy was performed. The tumoral mass was 2.5x2x1.5 cm in diameter, firm and well defined. Microscopically, the tumoral mass reflected a complicated fibrosing lipid necrosis with atypical endothelial and fibro-



**Figure 5.** Osteoid producing osteoblastic cells around the osteoid matrix within a spindle cell tumoral stroma (HEX20).



**Figure 6.** Diffuse vimentin expression in the spindle sarcomatoid stroma (X20).

blastic cells, demonstrating a final diagnosis of a benign pseudo-tumoral process. The patient is healthy, has received no adjuvant therapy, and no evidence of local or systemic disease was found after 16 months from initial surgery.

### Discussion

Phyllodes tumors are uncommon neoplasms that account for fewer than 1% of all breast tumors (7, 8). Osteosarcomatous differentiation of a malignant phyllodes tumor is also rare, accounting for 1.3% of the phyllodes tumors of the breast and it has been limited to case reports (4, 9). Osteosarcomatous differentiation in a malignant phyllodes tumor is mostly seen in middle and older age groups. The cases present as asymptomatic lumps, frequently in the upper outer quadrants, and have an almost equal distribution in both breasts. The size of the tumor varies from 2 to 40 cm in diameter (4, 6, 8). The present case was a 63 year-old lady with a painless 7 cm mass, located in the middle outer quadrants of her right breast.

According to Tavassoli (10), the osteosarcomatous component occupies a variable percentage of the stroma of the phyllodes tumor,

ranging from 25% to 100% of the neoplasm. In the majority of cases (86%), osteosarcoma involves at least 75% of the phyllodes tumor. The osteosarcomatous component can be divided into three subtypes: fibroblastic, osteoblastic and osteoclastic, with reports suggesting the fibroblastic subtype accounting for approximately 50% of all tumors. Telangiactatic differentiation can also be seen in some cases. Although small scattered areas of fibroblastic and telangiactatic components were seen, the osteosarcomatous stromal component was represented in more than 90% in our case.

The diagnosis of an osteosarcoma in association with a phyllodes tumor can be challenging and differentials such as a primary osteosarcoma of the breast or metaplastic changes in a carcinoma need to be excluded. It may be difficult to differentiate a pure osteosarcoma of the breast from one arising within a phyllodes tumor. Adequate sampling is important in reliably assessing the nature of mammary spindle cell tumors with osteoid or osseous differentiation. Pure primary osteosarcomas are almost entirely negative for epithelial markers, a feature that helps to distinguish them from matrix-producing mammary carcinomas (1, 4, 10). The latter often have areas of recognizable carcinoma. The existence of a metaplastic carcinoma with a prominent osseous component can be excluded by immunohistochemical staining using primary antibodies such as cytokeratin AE1/AE3, cell adhesion molecule 5.2, epithelial membrane antigen and vimentin (4).

Our case showed very focal positivity with keratin in the spindle fibroblastic sarcomatoid component, however, the biphasic nature of the lesion forming benign ductal elements and the absence of definitive area of invasive ductal carcinoma supported a phyllodes tumor with osteoblastic sarcomatoid differentiation. Generally, biphasic tumors are negative for estrogen and progesterone receptors, a characteristic also seen with our current study.

The prognosis of this uncommon tumor is unclear. In predicting the development of metastasis in malignant phyllodes tumors of the breast, Hawkins et al. emphasized the importance of the following features, including high mitotic count, stromal overgrowth, severe nuclear pleomorphism, and infiltrating margins (11). The mitotic count was higher than 5 per 10 HPF (6-8 per 10 HPF) with nuclear pleomorphism in this particular case. The presence of the stromal overgrowth was conspicuous along with the existence of focal infiltrative margins. The tumor was completely resected with free margins and there were neither local (axillary lymph nodes) nor distant metastasis.

The clinical course and therapy of the patients with primary osteosarcomas and malignant phyllodes tumors with osteosarcomatous differentiation are similar. They can be treated either with modified radical mastectomy, simple mastectomy or complete excision of the tumor. However, the effect of surgical modality on either local recurrence or overall survival has not been well-documented.

### Conclusion

Osteosarcomatous differentiation of the phyllodes tumor in the breast is rare, with only a few cases reported in the literature. Therefore, there is inadequate information regarding follow-up of patients on which to base appropriate management guidelines.

Despite this limitation, it is recognized as a potentially aggressive neoplasm. Management should be similar to that of other sarcomas of the breast, with mastectomy being the treatment of choice. It is important to distinguish such tumors from a metaplastic osteosarcomatous carcinoma as it would require similar treatment to a primary carcinoma of the breast, with a substantial role for lymph node dissection, chemotherapy, and radiotherapy.

Morphologic findings of this particular tumor are suggestive of more unfavorable prognosis than conventional malignant phyllodes tumors, therefore, appropriate patient follow-up is necessary.

#### Conflict of interest

No conflict of interest was declared by the authors.

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