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Case Report

Malignant phyllodes tumor with extensive lipomatous differentiation

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ABSTRACT

Phyllodes tumors are uncommon neoplasms of the breast. Lipomatous differentiation of malignant phyllodes tumor is a rare stromal alteration of this fibroepithelial tumor, demonstrated as a fat-containing mass on imaging. We present the case of a 46-year-old woman who was diagnosed with a malignant phyllodes tumor of the breast that demonstrated extensive lipomatous differentiation.

Introduction

Phyllodes tumor is a rare fibroepithelial neoplasm of the breast, more commonly seen in middle-aged women. The most common presentation is that of a rapidly growing, palpable mass. Phyllodes tumors may be classified as benign, malignant, or borderline, a distinction which is largely made histologically based on the degree of nuclear atypia, tumor border, stromal cellularity, and mitotic activity. While Ductal carcinoma in situ (DCIS), Lobular carcinoma in situ (LCIS), or invasive cancers may arise from the epithelial component of phyllodes tumors, the stromal component may contain heterologous elements such as adipose tissue, cartilage, bone, skeletal muscle, and fibrous tissue. Lipomatous differentiation within a phyllodes tumor is an uncommon stromal alteration. Herein, we present a case of malignant phyllodes tumor with extensive lipomatous differentiation in a 46-year-old woman.

Case report

A 46-year-old woman presented for a screening mammogram, reporting a new lump in her upper outer left breast. Mammogram demonstrated a 35-mm fat-containing, oval mass with circumscribed margins in the 3 o'clock left breast, 9 cm from the nipple which corresponded to the palpable mass reported by the patient (Figs. 1 and 2). Breast sonography revealed an oval, parallel, hyperechoic mass in the left breast, corresponding to the mammographic finding and region of palpable concern (Figs. 3 and 4).

The patient underwent an ultrasound-guided core needle biopsy which showed fragments of fibroadipose tissue containing multiple foci of hypercellular spindle cell proliferation associated with benign ducts and focal fat necrosis. There was significant nuclear atypia and a few mitoses were present. Immunohistochemical stains showed that the spin-

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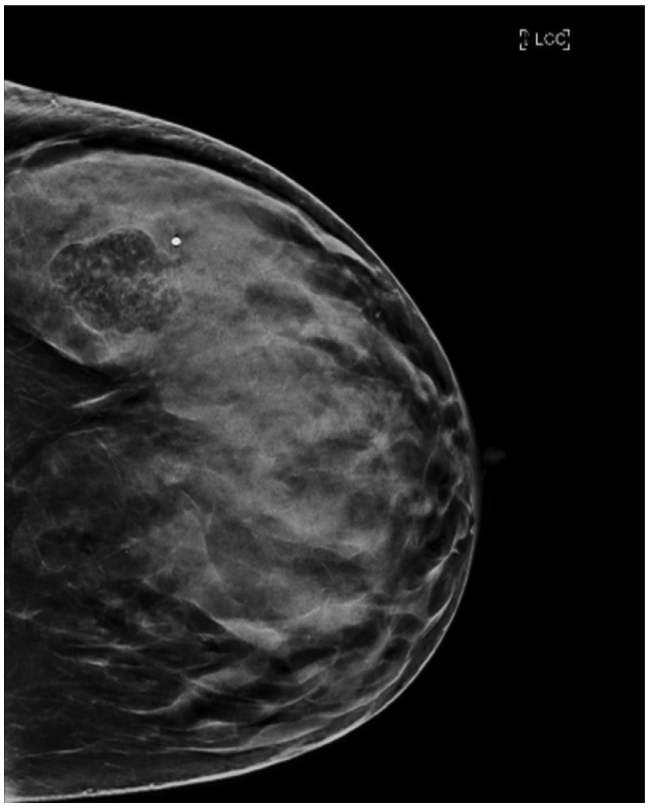

Fig. 1 – Craniocaudal digital breast tomosynthesis view of the left breast demonstrate a fat-containing, oval mass with circumscribed margins.

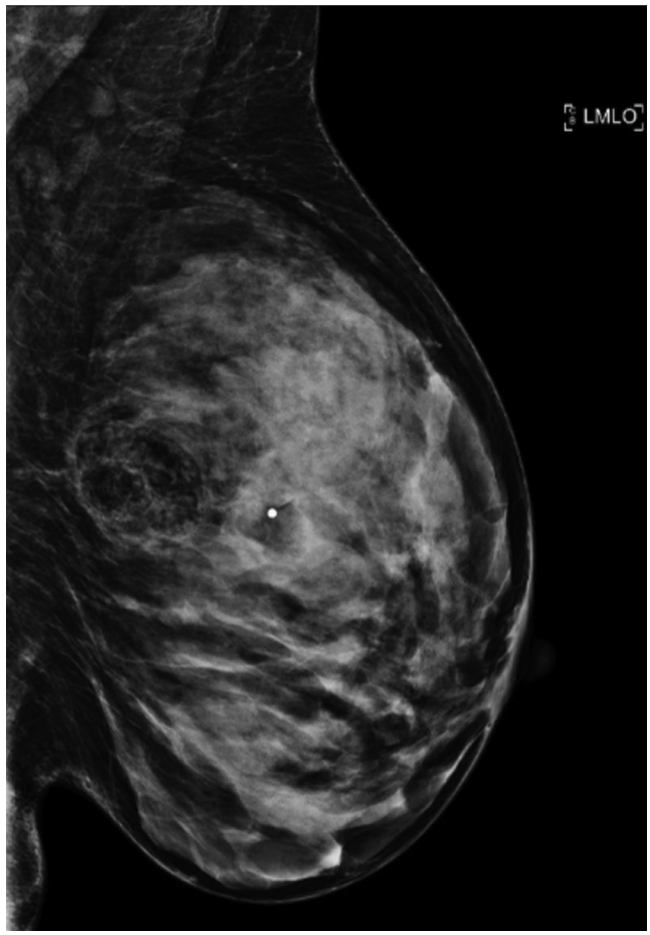

Fig. 2 – Mediolateral oblique synthetic digital breast tomosynthesis view of the left breast demonstrate a fat-containing, oval mass with circumscribed margins.

dle cells were negative for CK5/6, p63, CAM5.2, SMA, desmin, AE1/AE3, CD163, nuclear beta catenin, SMA, and CD34. The Ki-67 proliferation index was high (estimated ˜40%-60%). A definitive pathologic diagnosis was precluded in this specimen, and excision was recommended due to the presence of atypia, hypercellularity, and proliferation index (Fig. 5, 6 and 7).

Subsequent wire localization excisional biopsy was performed. Microscopic examination revealed a biphasic hypercellular lesion with both stromal and distorted glandular elements and extensive lipomatous differentiation. Although mostly well circumscribed, some infiltration into the surrounding tissue was identified as well as nuclear atypia and an increased mitotic rate (10 mitoses/High-power field (HPF)). The diagnosis of malignant phyllodes tumor with lipomatous differentiation was made based on these findings. Fluorescence in situ hybridization (FISH) was performed and was negative for Mouse double minute 2 (MDM2), suggesting that the lipomatous component itself was not malignant (ie, liposarcoma).

Discussion

Phyllodes tumors often present as a firm, palpable, mobile mass that demonstrates rapid growth often over a course of just several weeks. Imaging typically demonstrates a circumscribed, high density mass with oval, round, or lobulated shape. The mean size is 4-5 cm but can range from 1 to 20 cm. Associated calcifications are rare [1].

Certain imaging features of a phyllodes tumor may suggest malignancy. Partially obscured or indistinct tumor margins are more often seen in malignant phyllodes tumors. Tumor size of greater than 3 cm is associated with a higher likelihood of malignancy [1]. MRI may demonstrate restricted diffusion, suggestive of a malignant phyllodes tumor. Focal intralesional cysts are more common in malignant phyllodes tumors and are manifest on MRI by hyperintense slit-like spaces on T2-weighted images. While washout enhancement kinetics are suspicious for malignancy, up to 35% of the malignant phyllodes tumors may demonstrate persistent enhancement kinetics more typically associated with benignity [2].

Histologically, phyllodes tumors are biphasic, consisting of a hypercellular stromal component and cleft-like spaces lined by epithelium, often forming a leaflike pattern [3]. Sufficient sampling is necessary if the lesion appears ill defined (approximately 1 section per centimeter) and the tumor is classified based on the area of highest cellularity or floridity [4]. The tumors are divided into benign, intermediate, and malignant patterns based on several histologic characteristics, including an infiltrative margin, stromal overgrowth, mitotic count, amount of hypercellularity, and atypia [3].

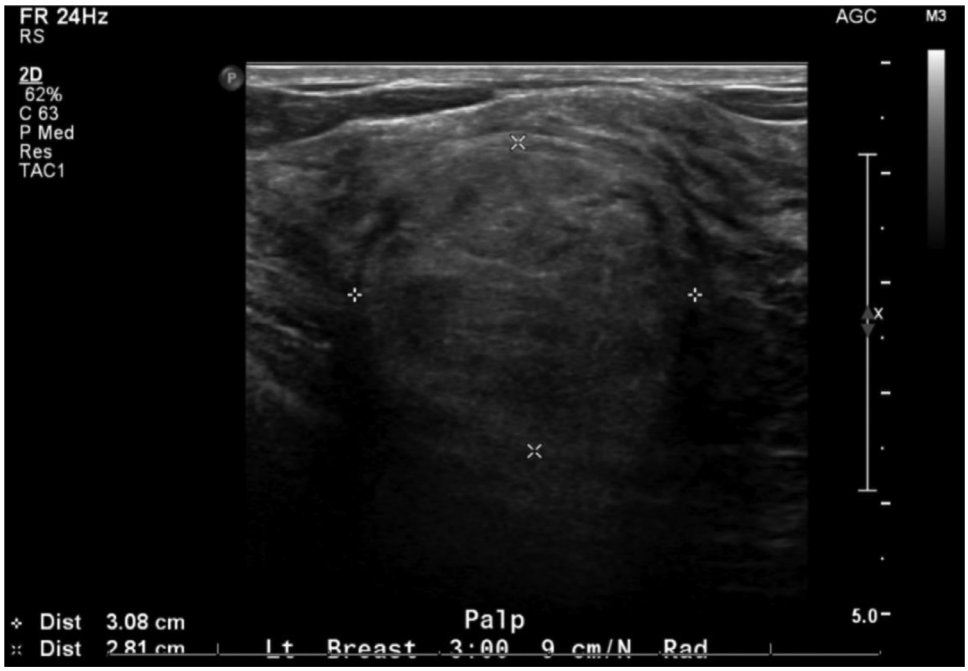

Fig. 3 – Radial grayscale ultrasound image of the left breast demonstrate an oval, parallel, hyperechoic mass corresponding to the mass seen on mammogram.

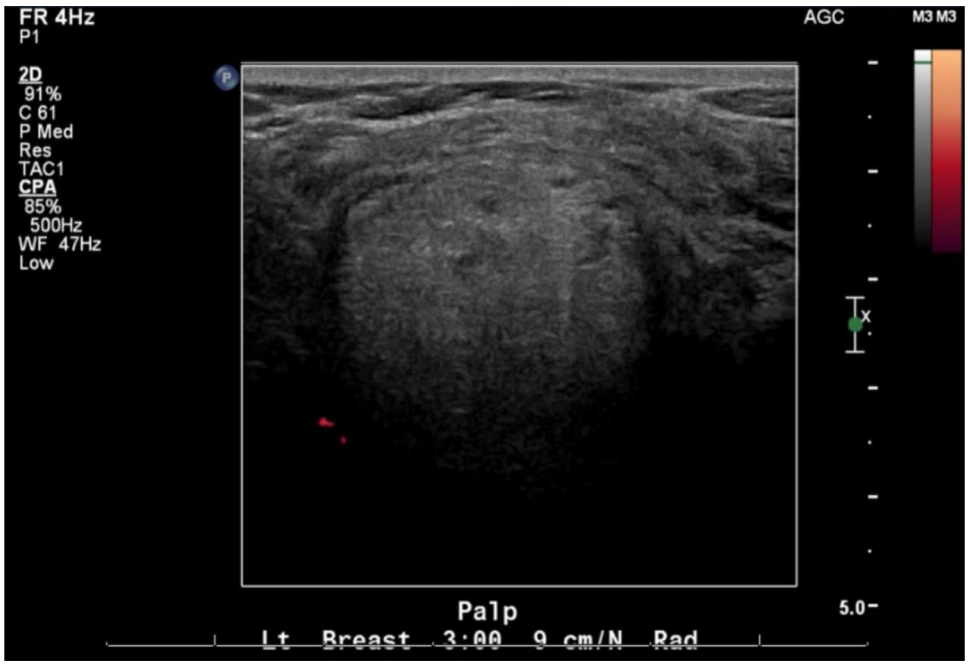

Fig. 4 – Power Doppler ultrasound image of the left breast demonstrate an oval, parallel, hyperechoic mass corresponding to the mass seen on mammogram, without significant internal vascularity.

Malignant transformation may occur in up to 20% of phyllodes tumors, often within its stromal component. Of those with malignant stromal differentiation, most display fibrosarcomatous components. Adipose stromal differentiation may also occur, ranging from mature fat to liposarcomatous transformation [5–8]. However, pure lipomatous differentiation is rare [9]. Powell and Rosen reported 14 cases of adipose differentiation, 13 of which were malignant [10].

One of the main differential considerations for a large, rapidly growing mass is fibroadenoma. As opposed to phyllodes tumors, fibroadenomas are more likely to contain calcifications, are less likely to contain cystic spaces and are usually

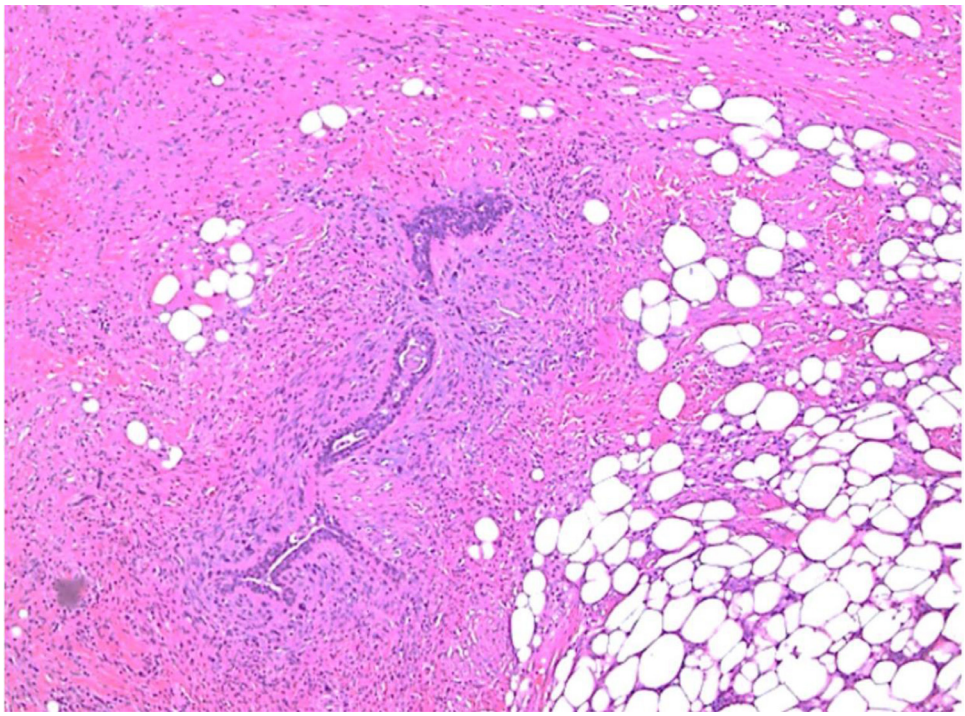

Fig. 5 – At 5x magnification, the lesion demonstrates a hypercellular stroma and distorted glandular elements with extensive lipomatous differentiation.

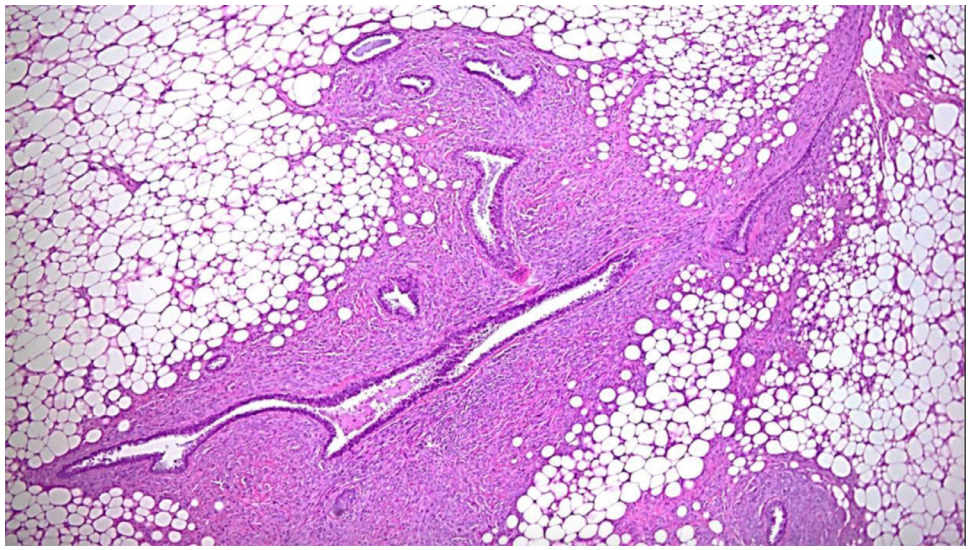

Fig. 6 – At 20x magnification, compression of the glands into cleft-like spaces by the stromal overgrowth is seen. Mature adipose tissue is present throughout the tumor.

uniform in stromal cellularity and distribution of stromal and glandular elements [3]. Fibroadenomas also typically occur in a younger subset of patients, with the mean age between 25 and 35. Overall, imaging alone cannot reliably distinguish fibroadenoma from phyllodes tumors. Additional differential considerations include metaplastic carcinoma, primary breast sarcoma, and periductal stromal sarcoma which are largely distinguished histologically.

Given the extensive fat present within the mass on imaging, another differential diagnosis is a hamartoma, which is a benign, well-circumscribed tumor composed of all components of breast tissue (fibrous, fibrocystic, and adipose tissue), resulting in a “breast-within-a-breast" appearance on mammography. Histologically, disordered breast ducts and lobules are present, unlike the phyllodes tumor which has epithelium lined spaces and stromal overgrowth. Unlike the malignant

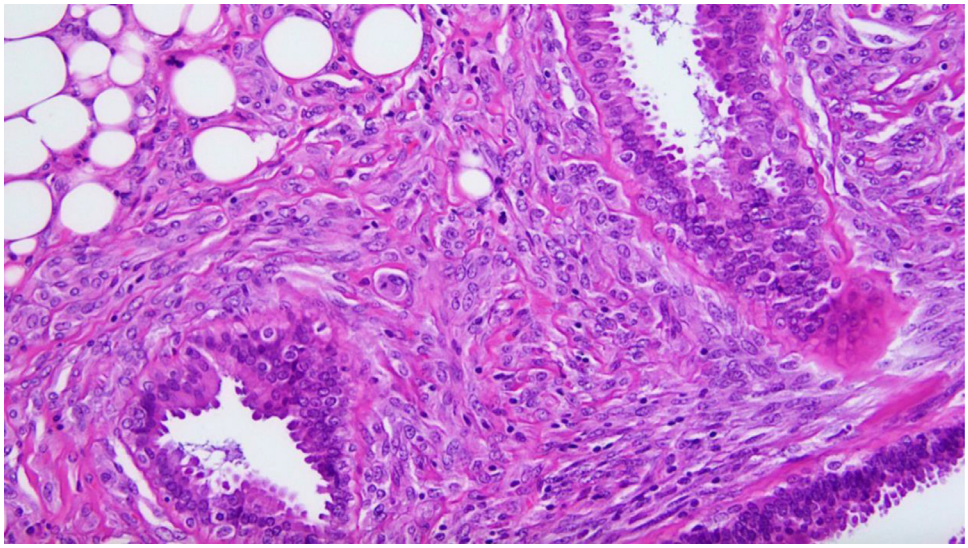

Fig. 7 – At 40× magnification, stromal cells are vesicular and pleomorphic with irregular nuclear contours and an increased nuclear to cytoplasmic ratio. Numerous mitotic figures are present.

phyllodes tumor, hamartomas consist of bland appearing cells without atypia [11]. Typically, fat-containing masses such as hamartomas are considered benign on imaging. Given that this mass was palpable and represented a mammographic change from prior studies, further evaluation with biopsy was warranted.

Management of both benign and malignant phyllodes tumors involves wide excision without axillary staging, with subsequent clinical follow-up for 3 years.

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